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FIG. 1A

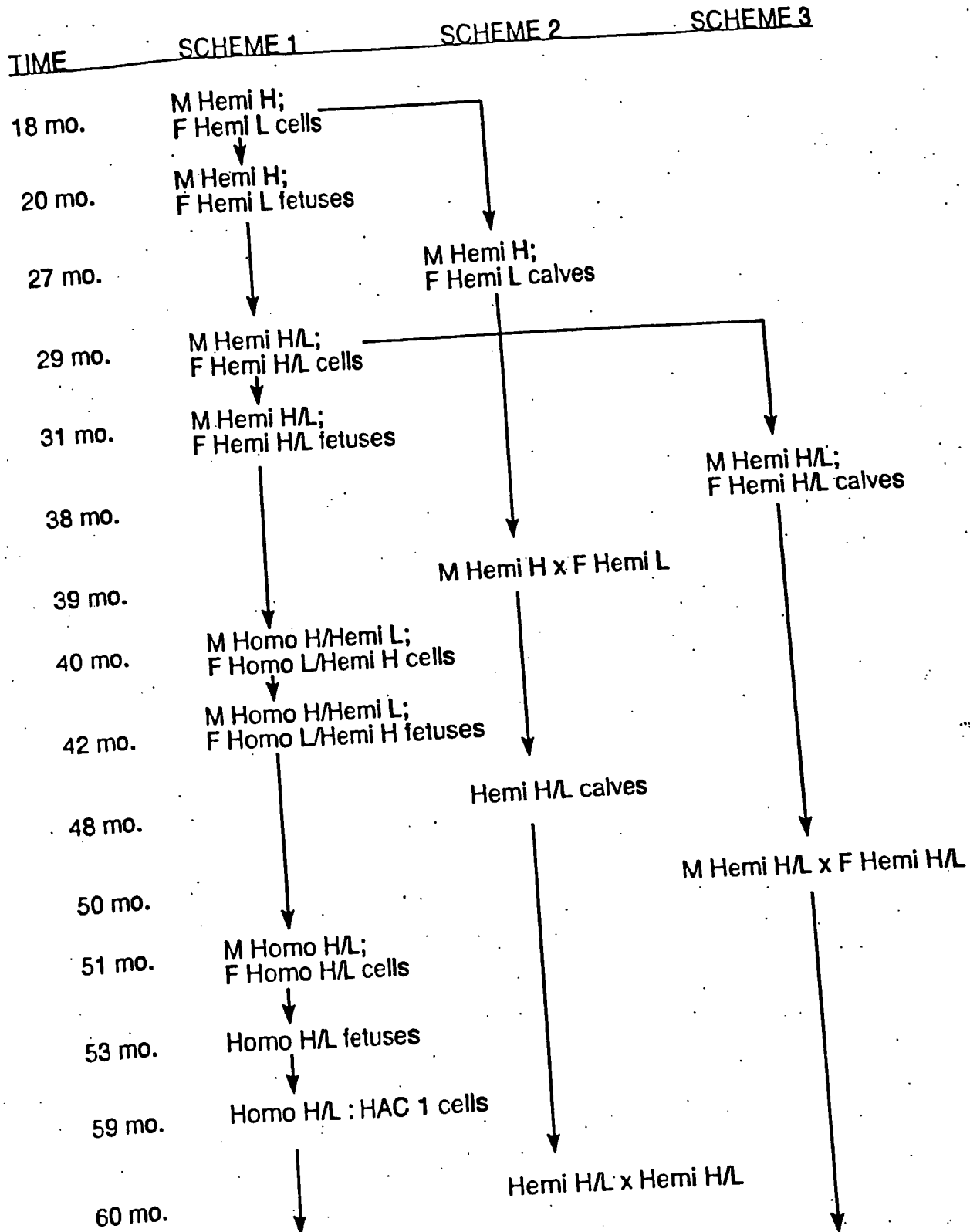


FIG. 1A (CONT.)

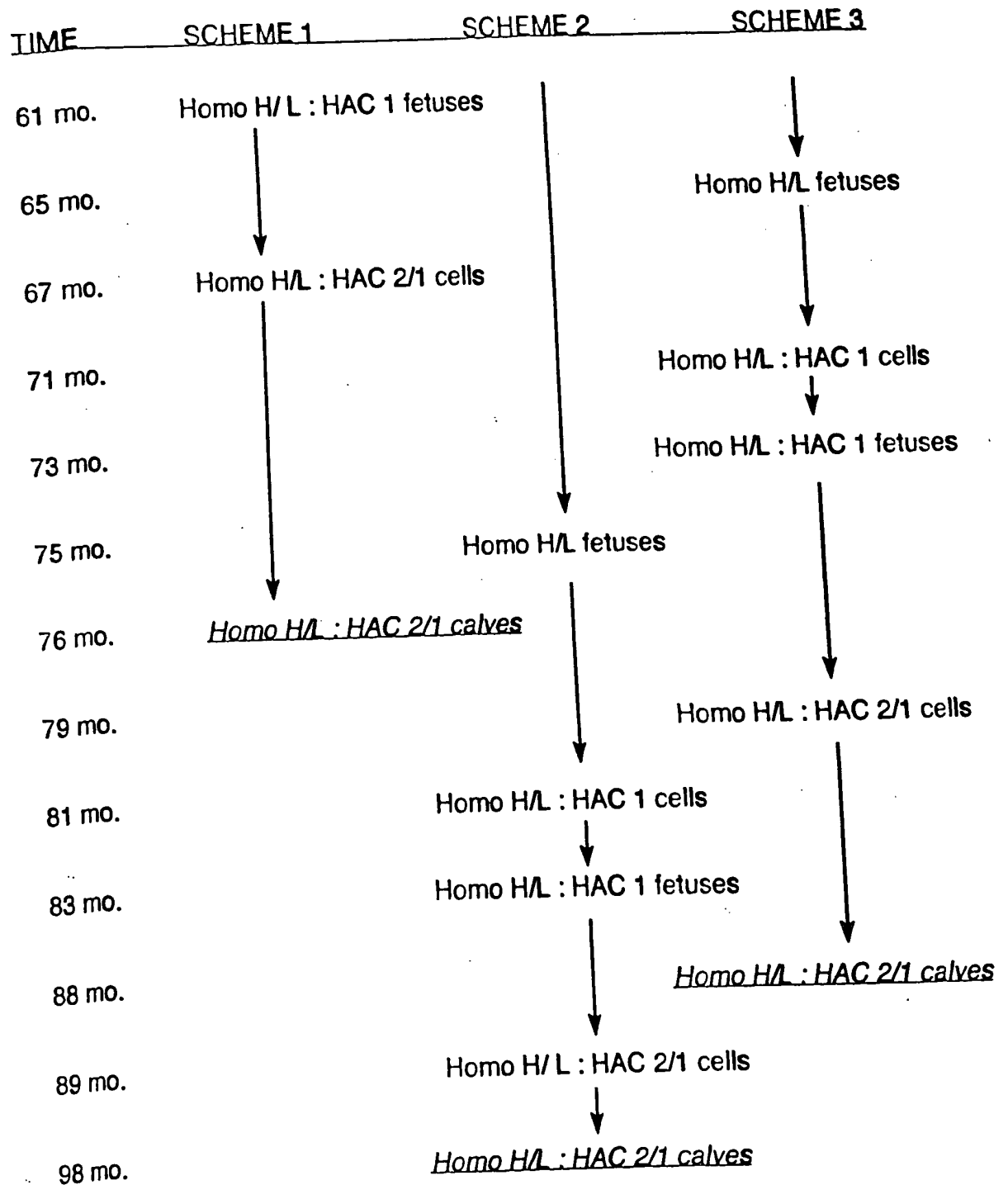


FIG. 1B

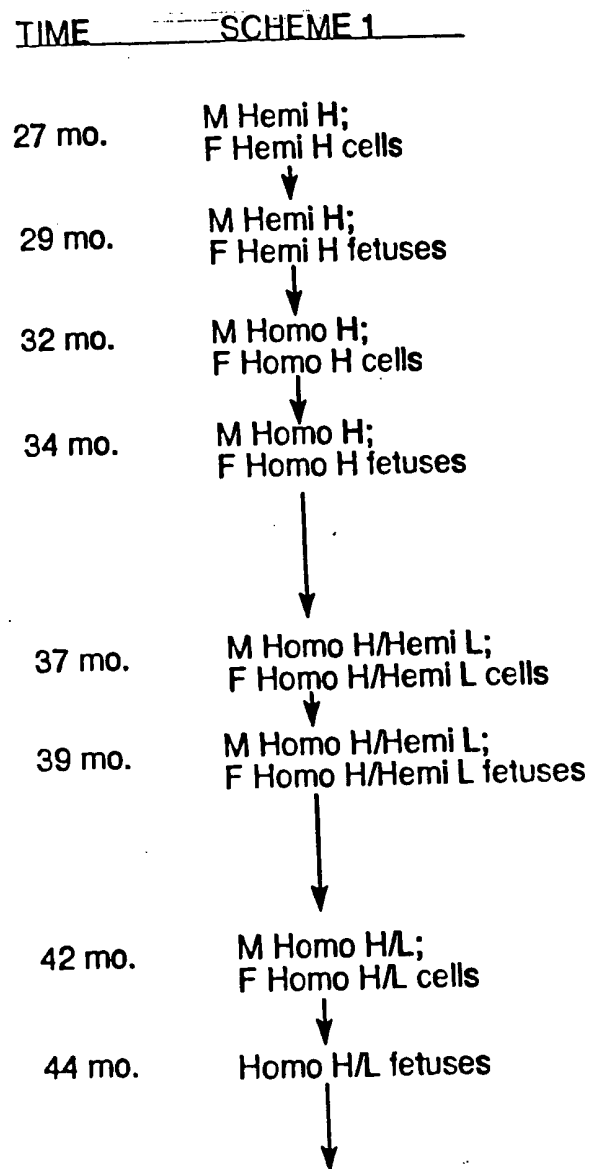


FIG. 1B (CONT.)

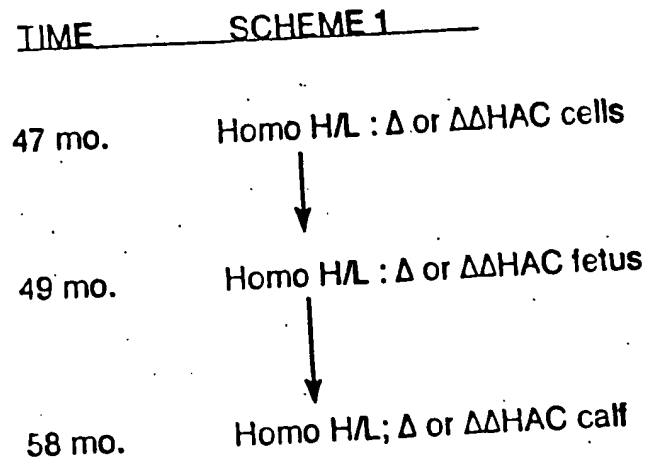


FIG. 2A

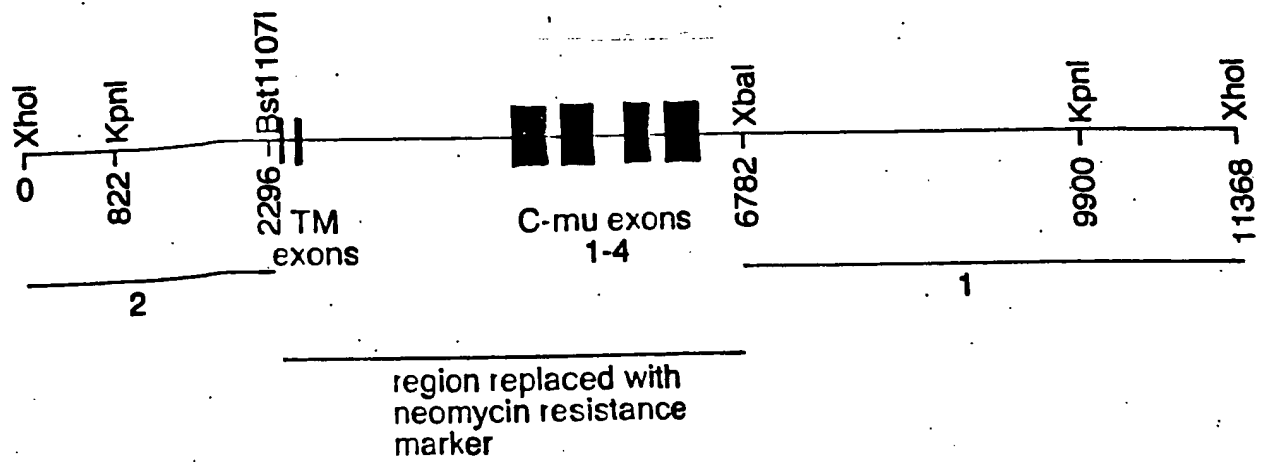


FIG. 2B

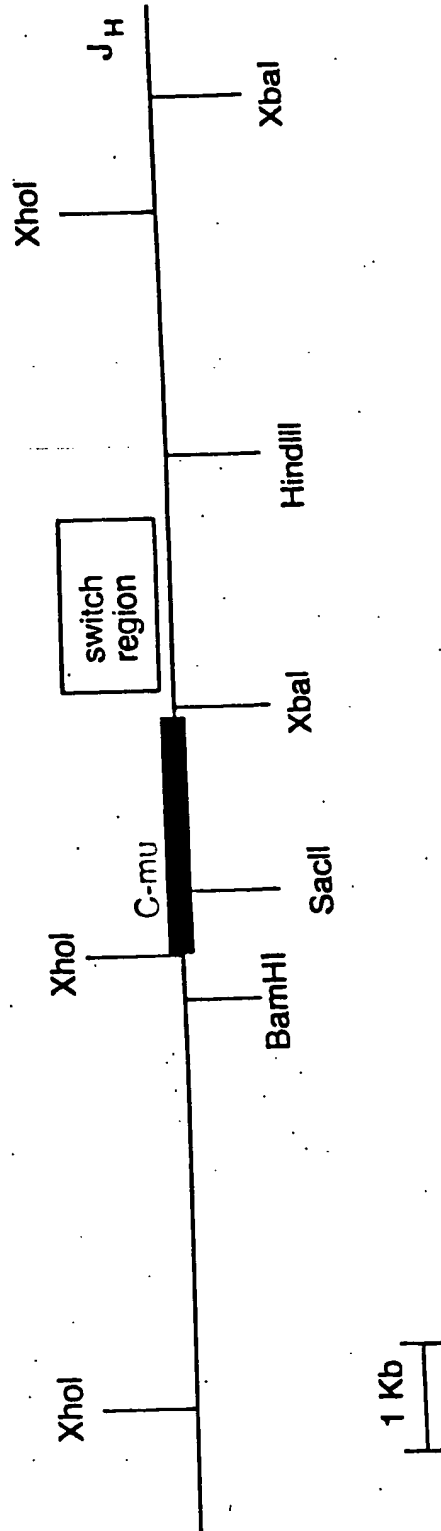


FIG. 3A

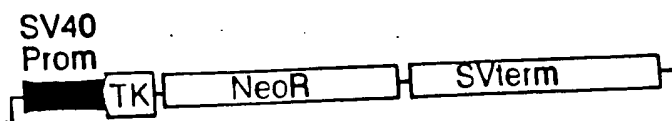


FIG. 3B

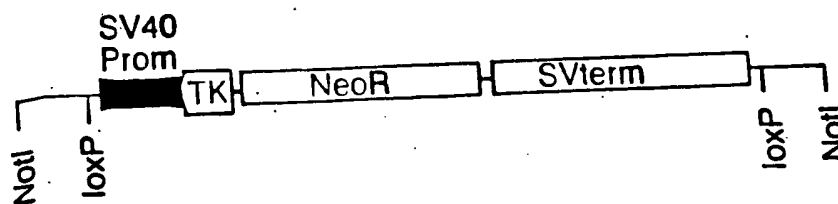
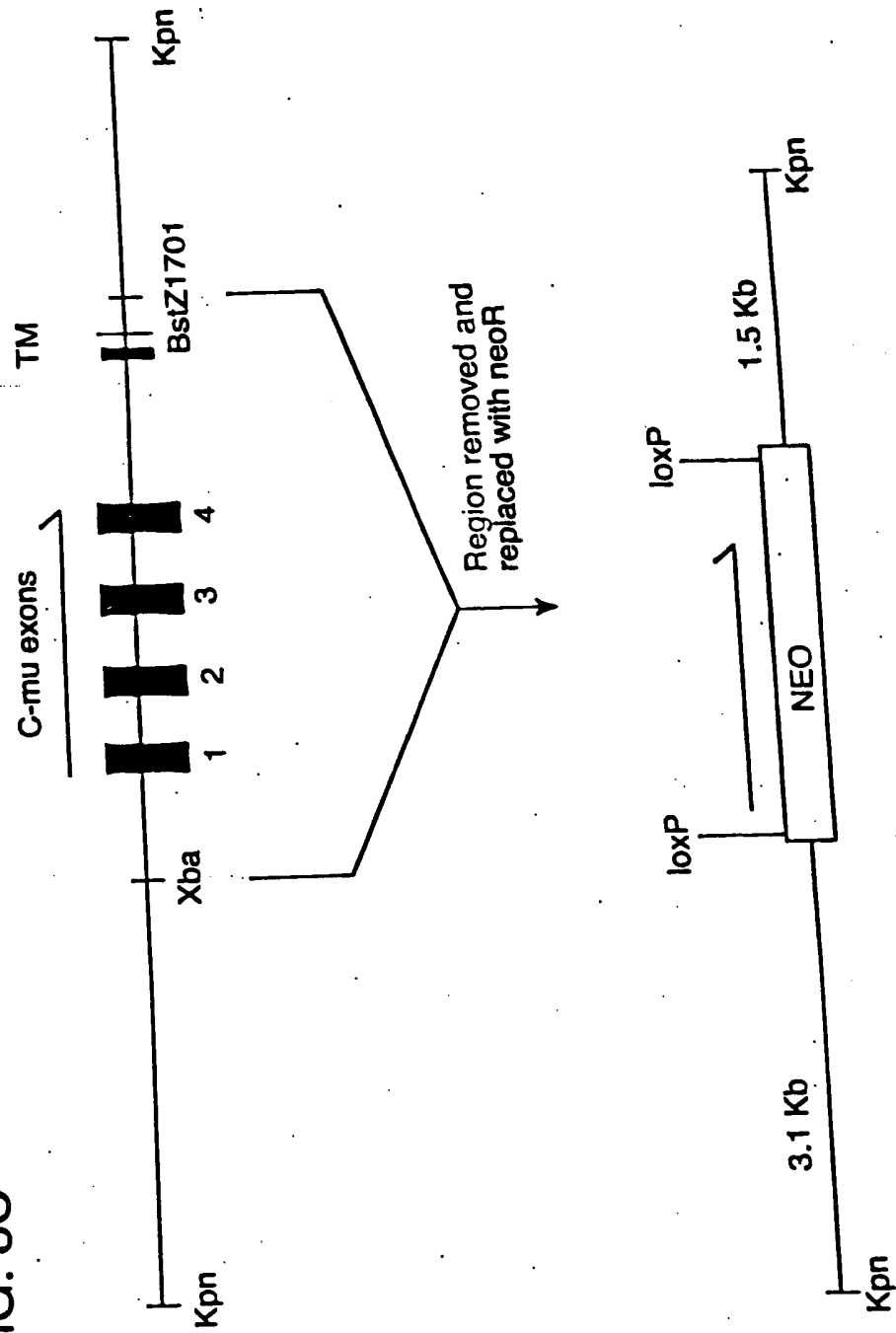




FIG. 3C



## FIG. 3D

SEQ ID NO:47

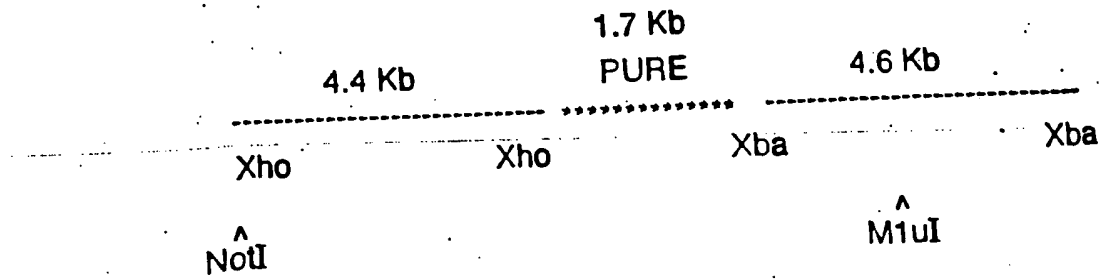
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cctgggtggccccacaagaggcgtcctgggaagccccagctccttccagccccgaaatgacctccctggagagccagatcac  
cctcaccagctccccctggccccagggtcctcctcctccatcccaccgcccaccctacctggcgttgccgtcacagctaa  
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cctgagacttcttccacctccaggcaccgttcttggcctgagggtgagggtcgcgctccctcaggggcacgatgtggctgca  
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gggaatggcggcagagagggcggggtgtccttggggctgtggcagggtctcatggatgcacacagcgggccccggctc  
aggccaccttgggaaaccagtcctgggactgcaactcggccatgttctgcatctggaccagccccaaagacaccacccggc  
gtggcggcacgtggcctgggaggagacacatgtccttctccatcagcaatgggttcagcactaggatatgcagcacacaggag  
tggtgtgggggtaaaaaaccttcacgagggaagcggttcacaaaaataaagta

FIG. 3E

SEQ ID NO: 48

[illegible]

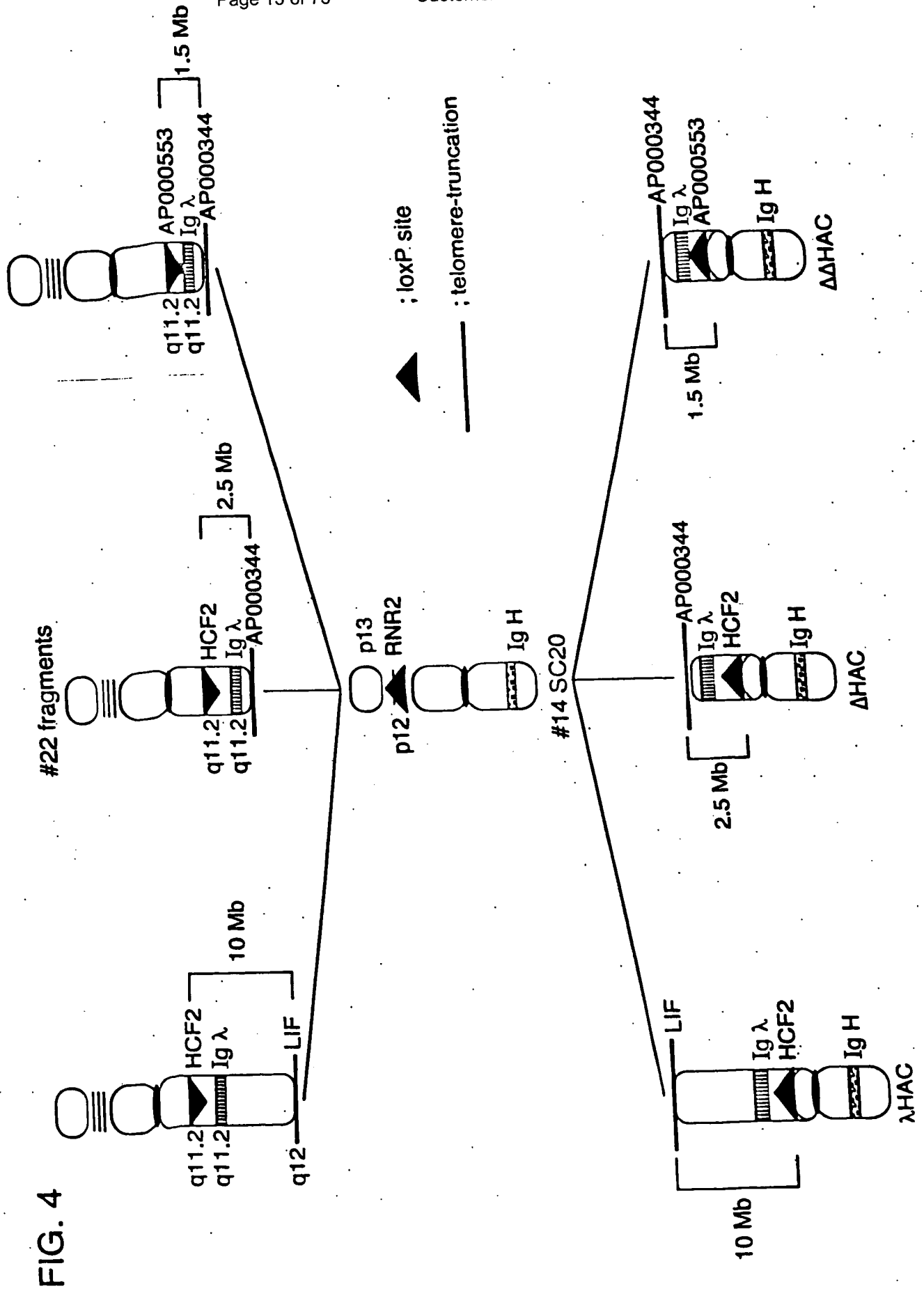
FIG. 3F



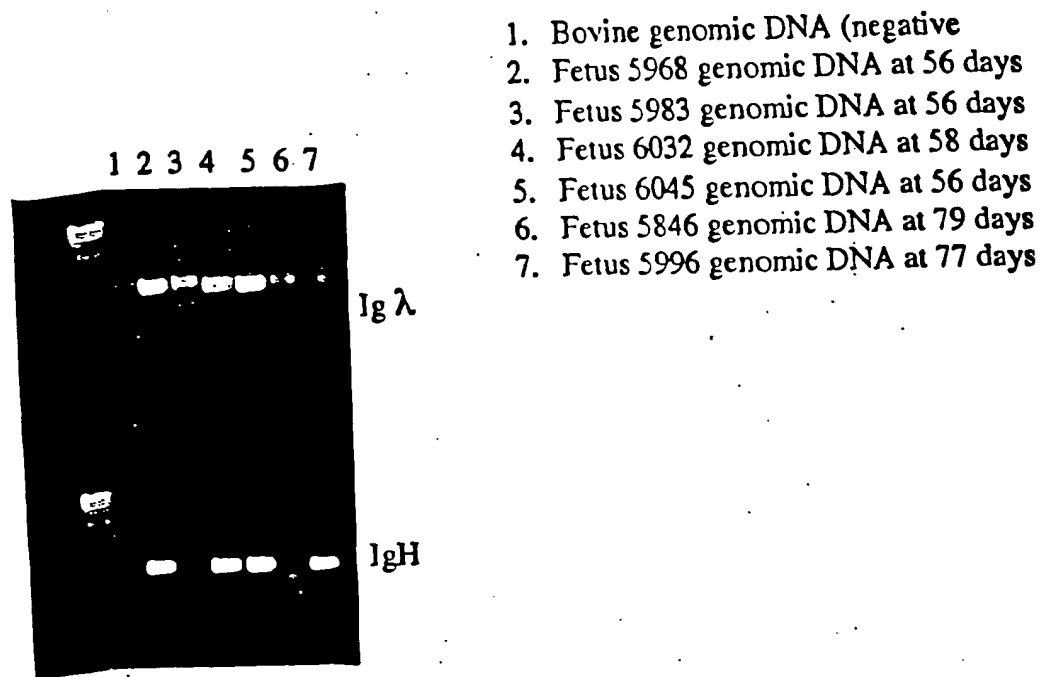
## FIG. 3G

SEQ ID NO: 60

1 atgagatcc ctgcicagct cctggggctc ctctgctct gggtcccagg  
51 atccagtgagg gatgtgtgc tgaccagac tccccctcc ctgctatca  
101 tccctggaga gacggctcc atctctgca agtctactca gagtctgaaa  
151 tatagtgat gaaaaaccta mgtactgg ctcaacata aaccaggcca  
201 atcaccacag ctgtgatct atgctgttc cagccgtac actggggctc  
251 cagacaggt cactggcagt gggtcagaaa cagattcac acttacgatc  
301 aacagtgtgc aggtgagga tgtggagtc tattactgtc tcaaacaac  
351 atatgtcca aatacttcg gccaaaggaa caaggtagag atcaaaagg  
401 ctgatgtga gccatcgtc tccctctca aaccatctga tgagcagctg  
451 aagaccgaa ctgctctgt cgtgtgctt gtagatgatt tctaccccaa  
501 agatatcaat gtcaagtga aagtggatgg ggtactcag agcagcagca  
551 acttcaaaa cagttcaca gaccaggaca gcaagaaaag cacctacagc  
601 ctacgagca tctgacact gccagctca gatlacaaa gccatgacgc  
651 ctatcgtgt gaggtcagcc acaagagcct gactaccacc ctgtcaaga  
701 gcttcagtaa gaacgagtgt tag

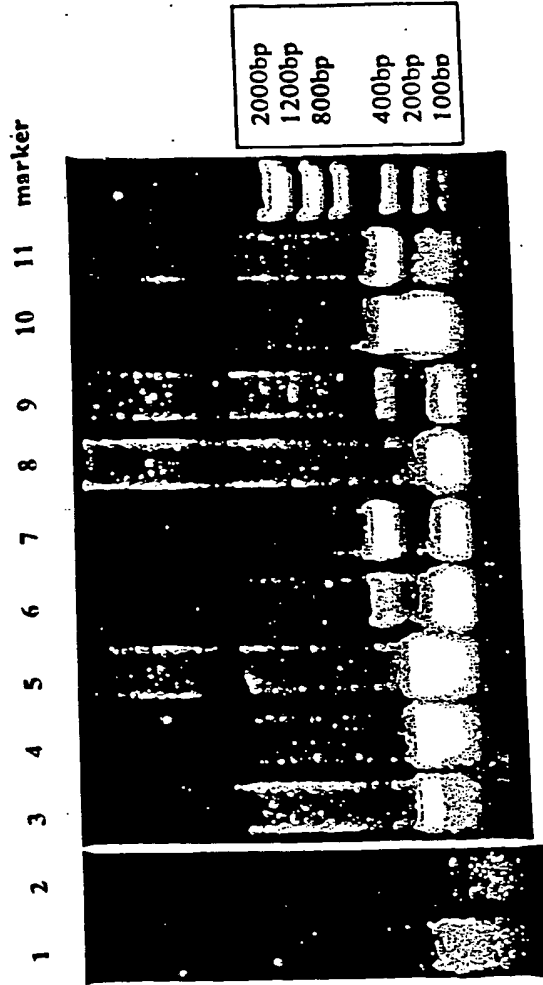


**FIG. 5**



Fetus	Clone	IgH	Ig $\lambda$
5968	B4-2	Pos	Pos
5983	B2-13	Neg	Neg
6032	B4-8	Pos	Pos
6045	B2-22	Pos	Pos
5846	B4-8	Neg	Neg
5996	B4-2	Pos	Neg

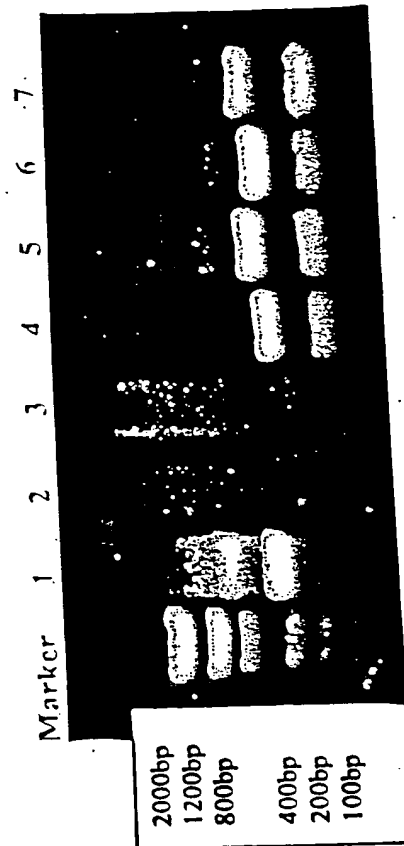
FIG. 6



1. Human mu constant region in bovine liver cDNA from fetus 5996.
2. Human mu constant region in bovine brain cDNA from fetus 5996.
3. Human mu constant region in bovine spleen cDNA from fetus 5996.
4. Human mu constant region in human spleen cDNA.
5. Human mu constant region in mouse spleen cDNA with HAC.
6. Bovine rearranged Cmu heavy chain in bovine spleen cDNA from fetus 5996.
7. Bovine rearranged Cmu heavy chain in human spleen cDNA.
8. Bovine rearranged Cmu heavy chain in mouse spleen cDNA with HAC.
9. GAPDH primers in bovine spleen cDNA from fetus 5996.
10. GAPDH primers in bovine liver cDNA
11. GAPDH primers in mouse spleen cDNA with HAC.



FIG. 7



1. GAPDH primers in bovine liver cDNA
2. Bovine rearranged Cmu heavy chain in bovine brain cDNA from fetus 5996.
3. Bovine rearranged Cmu heavy chain in bovine liver cDNA from fetus 5996.
4. GAPDH primers in bovine spleen cDNA from fetus 5996.
5. Bovine rearranged Cmu heavy chain in bovine spleen cDNA from fetus 5996.
6. GAPDH primers in bovine brain cDNA from fetus 5996.
7. Bovine rearranged Cmu heavy chain positive control.

FIG. 8

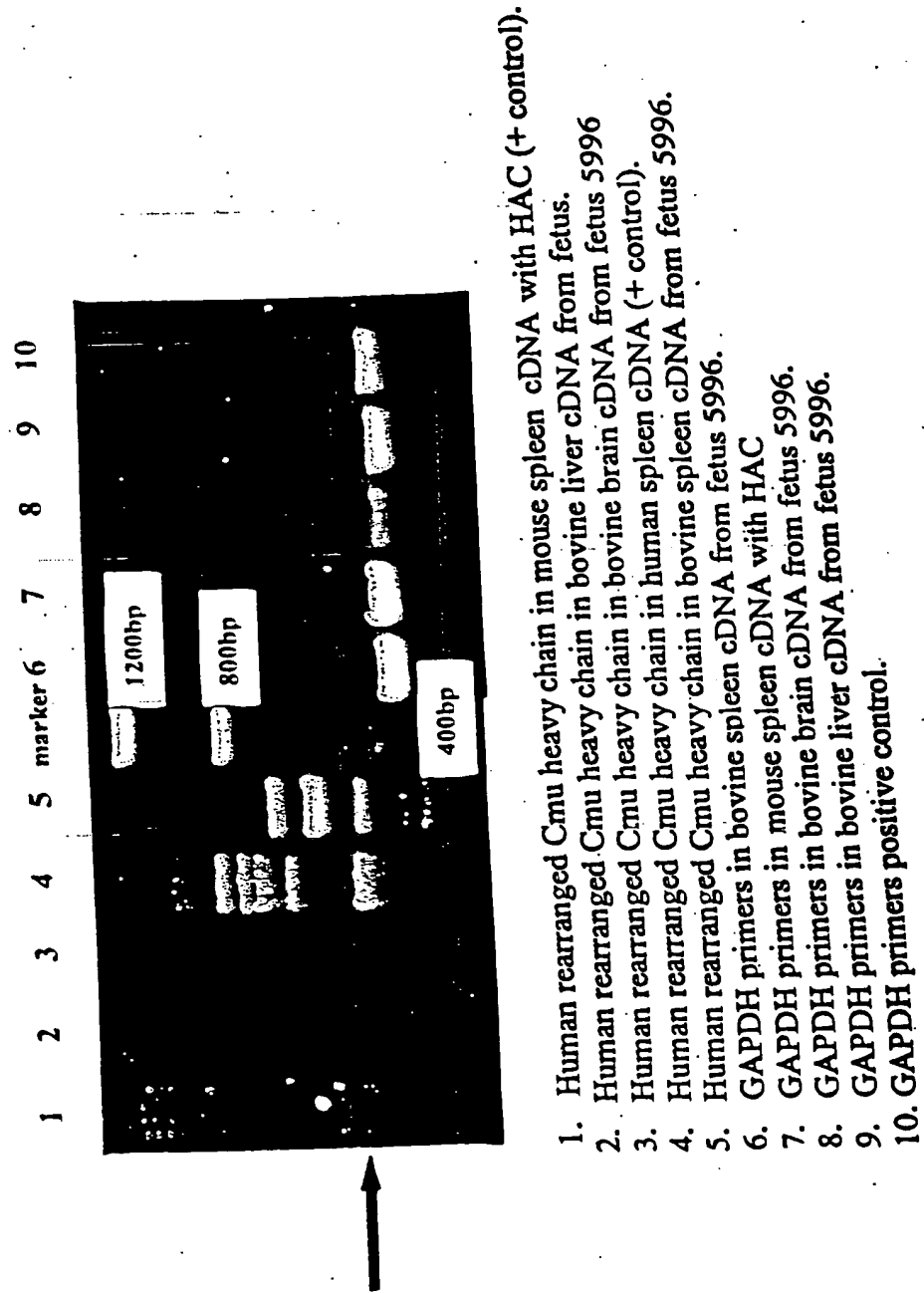


FIG. 9

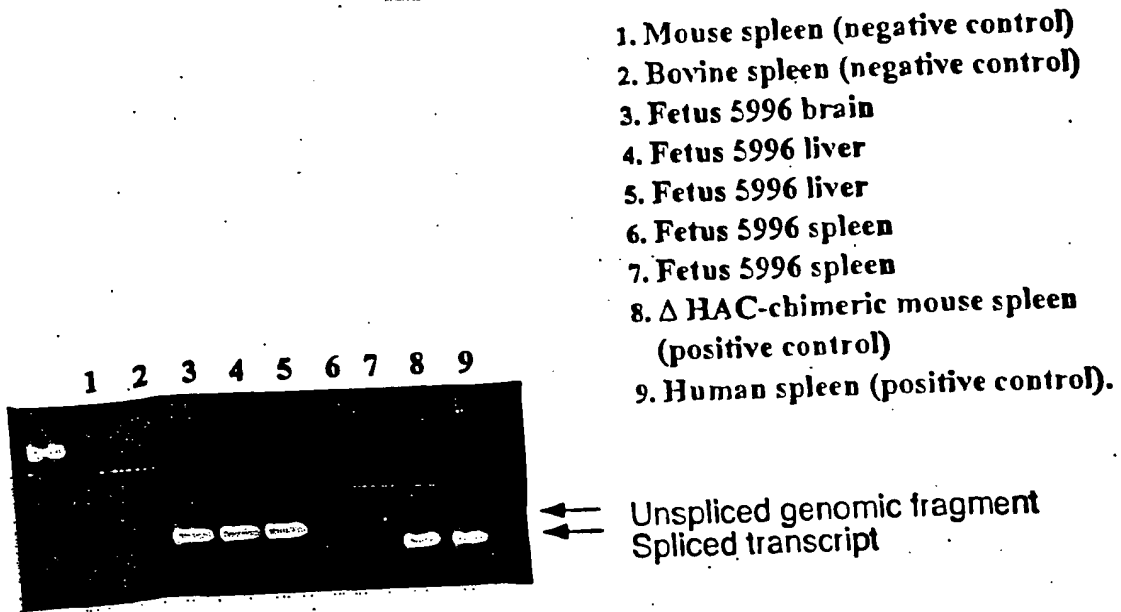
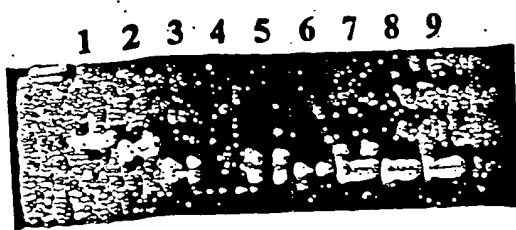


FIG. 10



1. Mouse spleen (negative control)
2. Bovine spleen (negative control)
3. Fetus 5996 brain
4. Fetus 5996 liver
5. Fetus 5996 liver
6. Fetus 5996 spleen
7. Fetus 5996 spleen
8.  $\Delta$ HAC-chimeric mouse spleen  
(positive control)
9. Human spleen (positive control)

FIG. 11A

SEQ ID NO: 49

5'  
GGGAAGG AAGTCCTGTGGGACCANCCAACGGGCCACGCTGCTCGTATCCGACG  
GGGAATTCTCACAGGAGACGAGGGGGAAAAGGGTTGGGGCGGATGCACTCC  
CTGAGGAGACGGTGACCAGGGTTCCNTGGCCCCAGNNGTCAAA3'

FIG. 11B

SEQ ID NOs: 50 and 51

V-D-J region

→ constant mu region

Subject: 5'

tttgactactggggccagggaaccctggtcaccgtctcctcagggagtgcatccgccccca  
-----nn-----n-----

Query

Subject:

acccttttccccctcgtctcctgtgagaattccccgtcggatacagagcagcgtggccggtt  
-----

Query

Subject: 5'

ggctgcctcgcacaggacttccttccc gactccatcactttctectg 3'  
-----g----- Cmul primer

SEQ ID NOs: 52 and 53					
55	46	37	28	19	10
GGA GGC TTG GTC AAG CCT GGA GGG TCC CTG AGA CTC TCC TGT GCA GCCTCTT GGA					
G G L V K P Q G S L R L S C A A S O					
109	100	91	82	73	64
TTCACCTTCAGTGACTACTATCATGAGCTGGATCCGCCAGGCTCCA GGG AAG GGG					
P T F S D Y Y M S W I R Q A P Q K G					
163	154	145	136	127	118
CTGGAGTGG GTTTCA TACAATTAGTAGTGGTAGTGGTAGTACCATA TACTACGCA GAC					
L B W V S Y I S S S G S T I Y Y A D			VH3-11		
217	208	199	190	181	172
TCTGTGAAG GGCCGA TTC ACC ATCTCCAGG GACAACGCC AAGAACTCA CTGTAT					
S V K G R F T I S R D N A K N S L Y					
271	262	253	244	235	226
CTGCAAATG AACAGCCTGAGA GCCGAGGACACGGCTGTGTATTACTGT GCGAGA					
L Q M N S L R A E D T A V Y C A R					
325	316	307	298	289	280
ATA ACT GGGGATGCTTTT GAT ATCTGGGGC CAAGG ACA ATG GTCACCGCTCTCT					
I T G D A F D I W G Q G T M V T V S		JH3			
379	370	361	352	343	D7-27
TCA GGG AGT GCA TCCGCCCCA ACCCTTTTCCTTCCTCCTCCTCTGTGTGAG AATTCC					
S G S A S A P T L F P L V S C B N S					
388	Cμ				
388	CCCTCG GAT ACG AGC 3'				
	P S D T S				

FIG. 12A

FIG. 12B

SEQ ID NOS: 54 and 55

5' GTG GAG TCT GGG OGA GGC TTG GTA CAG CCT GGG AGG TCC CTG AGA CTC TCC TGT  
V B S O O O L V Q P G R S L R L S C

OCA GCG TCA GGA TTC ACC TTC AGG AAC TTG GGC ATG CAC TGG GTC CGC CAG GCT  
A A S G F T P R N P G M H W V R Q A

CCA GGC AAG GGG CTG GAG TGG GTG ACA GTT ATA TGG TAT GAC GGA AGT AAT CAA  
P G K G L E W V T V I W Y D G S N Q

TACTAT ATA GACTCC GTG AAG GGC CGA TTC ACC ATC TCC AGA GAC AAT TCC AAG  
Y Y I D S V K G R F T I S R D N S K

AAC ATG TTG TAT CTG CAA ATG AAC AOC CTG AGA GCC GAG GAT ACG GCT GTG TAT  
N M L Y L Q M N S L R A B D T A V Y

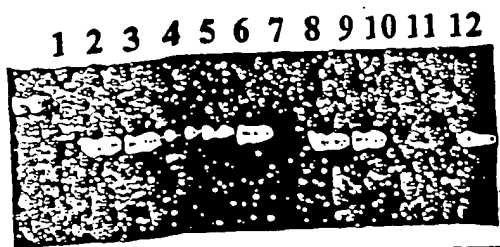
TACTGT GCG AGA GAT CGC AAT GGC CTG AAG TACTTTC GAT CTC TGG GGC CGT GGC  
Y C A R D R N G L K Y F D L W G R G

ACC CTG GTC ACT GTC TCA TCA GGG AGT GCA TCC CTC CCA ACC CTC TTC TTC C C C  
T L V T V S S G S A S A P T L P P L

GTC TTC TGT GAG AAT TCC CTC GTC GAT ACG AGC J  
V S C E N S P S D T S

D6-39 ? N addition JH2 Cμ

FIG. 13

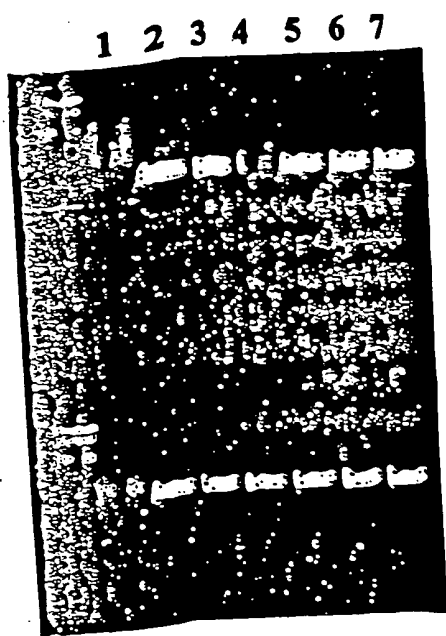


Fetus	Clone	IgH	Igλ
5580	412	Pos	Pos
5848	214	Neg	Neg

1. Bovine genomic DNA (negative control)
2. Fetus 5580 genomic DNA (Igλ)
3. Fetus 5580 genomic DNA (Igλ)
4. Fetus 5848 genomic DNA (Igλ)
5. Fetus 5848 genomic DNA (Igλ)
6. Positive control (Human genomic DNA)
7. Bovine genomic DNA (negative control)
8. Fetus 5580 genomic DNA (IgH)
9. Fetus 5580 genomic DNA (IgH)
10. Fetus 5848 genomic DNA (IgH)
11. Fetus 5848 genomic DNA (IgH)
12. Positive control (Human genomic DNA)



**FIG. 14**



**IgH**

1. Bovine genomic DNA (negative control)
2. Fetus 5442A genomic DNA (91 day)
3. Fetus 5442A genomic DNA (91 day)
4. Fetus 5442B genomic DNA (91 day)
5. Fetus 5442B genomic DNA (91 day)
6. Fetus 5968 genomic DNA (56 day; positive control)
7. Human genomic DNA (positive control)

**Igλ**

FIG. 15

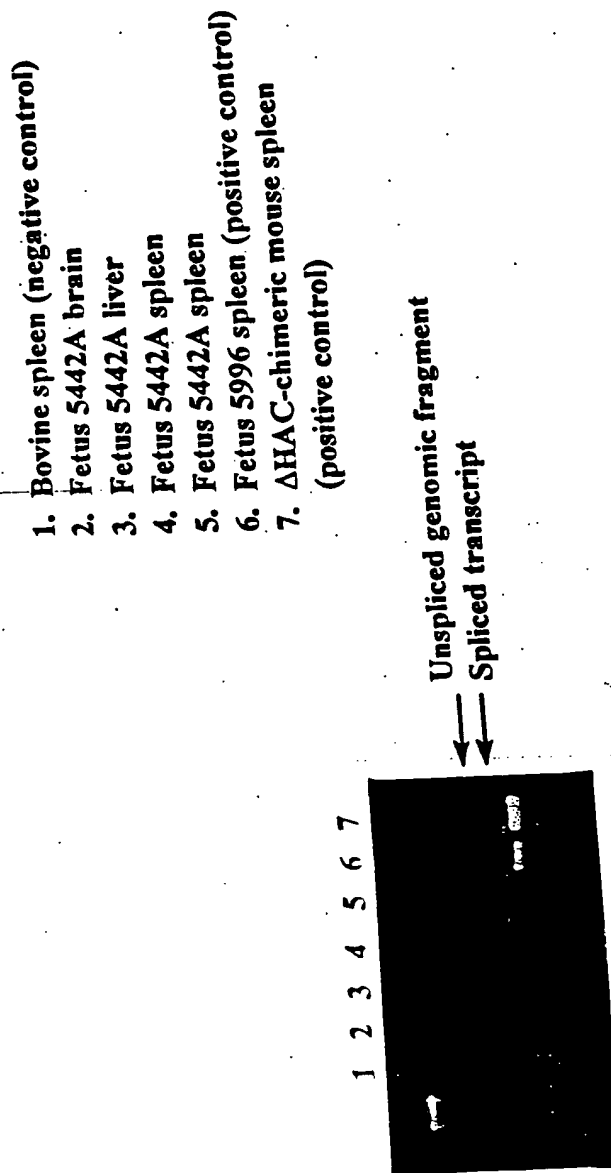
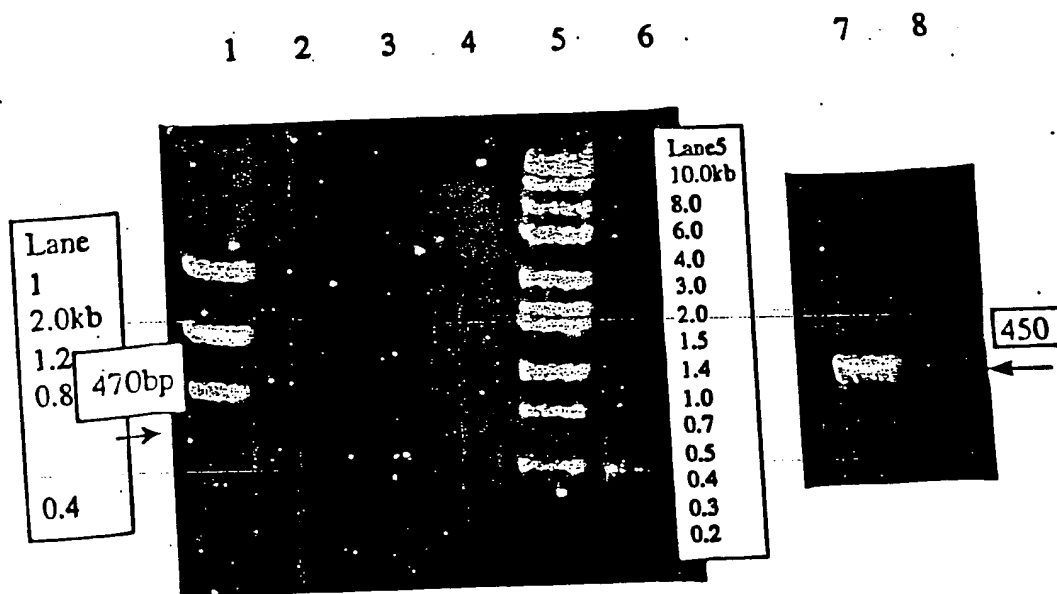


FIG. 16



1. Low Mass Ladder: 2.0, 1.2, 0.8, 0.4, 0.2  
0.1kb

2. Normal Bovine spleen cDNA negative

3.  $\Delta\Delta$ HAC 5868A spleen

4. empty

5. Hi Lo

0.2, 0.1kb

6. Tc Mouse HAC spleen cDNA positive

7. GAPDH product from 5868A spleen cDNA

8. GAPDH product from normal bovine  
cDNA

FIG. 17

1. Bovine spleen (negative control)
2. Fetus 5442A brain
3. Fetus 5442B brain
4. Fetus 5442A liver
5. Fetus 5442B liver
6. Fetus 5442A spleen
7. Fetus 5442A spleen
8. Fetus 5442B spleen
9. Fetus 5442B spleen
10.  $\Delta$ HAC-chimeric mouse spleen (positive control)

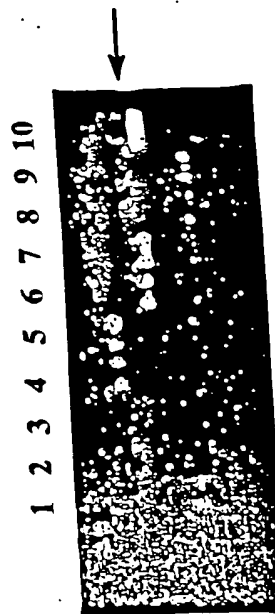


FIG. 18

1. Bovine spleen (negative control)
2. Fetus 5442A brain
3. Fetus 5442A liver
4. Fetus 5442A spleen
5. Fetus 5442A spleen
6.  $\Delta$ HAC-chimeric mouse spleen (positive control)

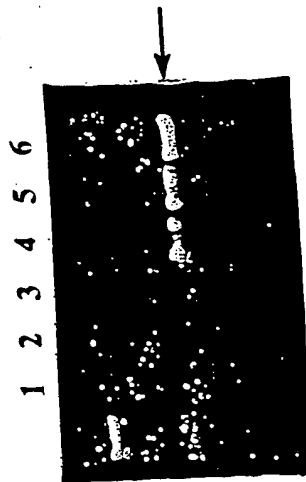


FIG. 19

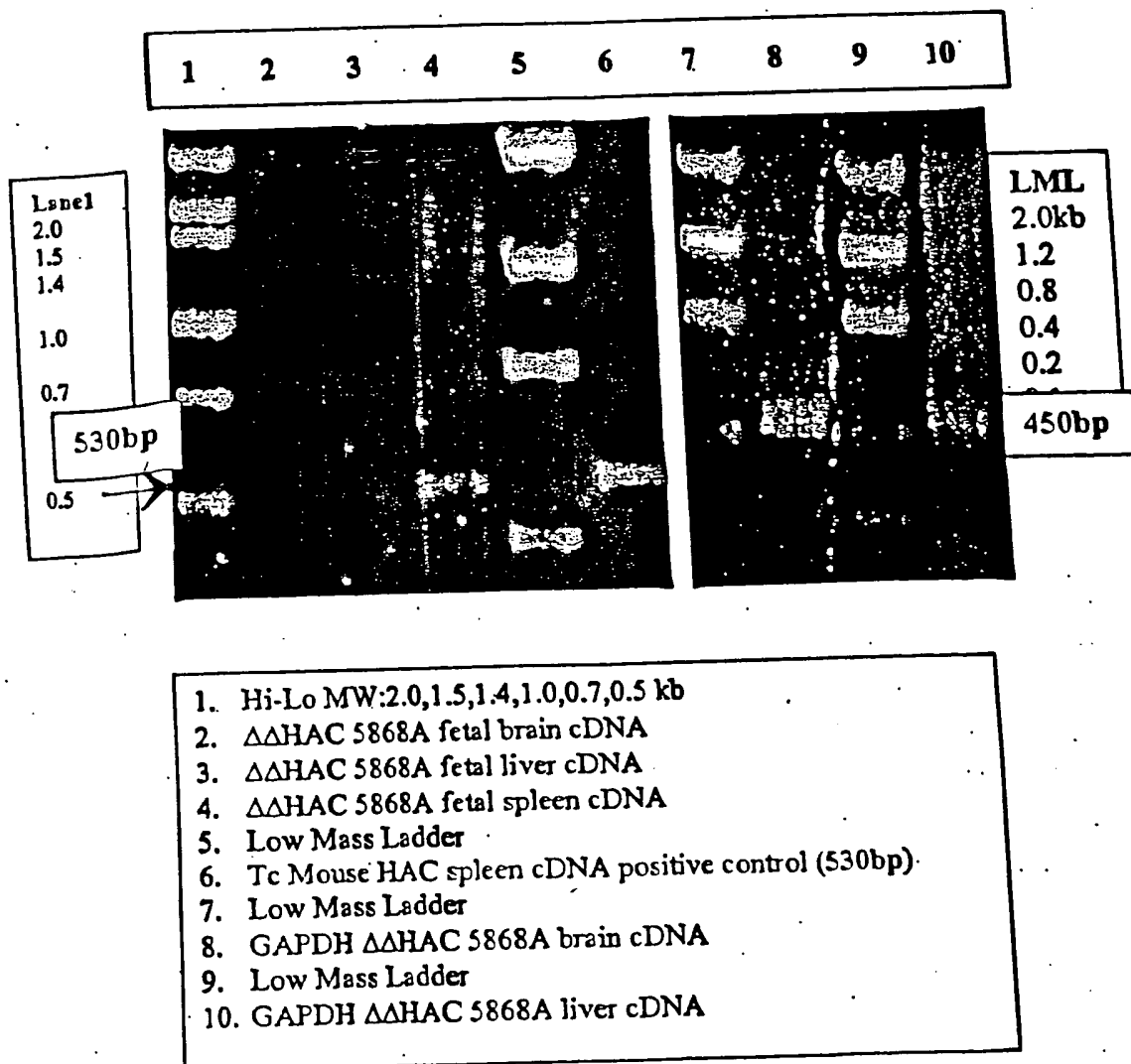


FIG. 20

SEQ ID NOs: 56 and 57

```
5' ACC CTC CTC ACT CACTGT GCA GGG TCCTGG GCC CAGTCT GTG CTG ACT CAG CCA  
T L L T H C A G S W A Q S V L T Q P  
CCCTCA GCG TCT GGG ACC CCC GGG CAG AGG GTC ACC ATC TCT TGT TCT GGA AGC  
P S A S G T P G Q R V T I S C S G S  
AGCTCC AAC ATC GGA AGT AATTAT GTA TACTGG TACCAG CAG CTC CCA GGA ACG  
S S N I G S N Y V Y W Y Q Q L P G T  
GCC CCC AAA CTC CTC ATC TAT AGG AAT AAT CAG CGG CCCTCA GGG GTC CCT GAC V1-17  
A P K L L I Y R N N Q R P S G V P D  
CGA TTC TCT GGCTCC AAG TCT GGC ACCTCA GCC TCC CTG GCC ATC AGT GGG CTC  
R F S G S K S G T S A S L A I S G L  
CGG TCC GAG GAT GAG GCT GAT TAT TACTGT GCA GCA TGG GAT GAC AGC CTG AGT  
R S E D E A D Y Y C A A W D D S L S  
GGT CTT TTC GGC GGA GGG ACC AAG CTG ACC GTC CTA GGT CAG CCC AAG GCT GCC  
G L F G G G T K L T V L G Q P K A A  
CCCTCG GTC ACT CTG TTC CCA CCC TCC TCT GAG GAG CTT CAA GCC AAC AAG GCC  
P S V T L F P P S S E E L Q A N K A  
JL3  
ACA CTG GTG 3'  
T L V
```

FIG. 21

SEQ ID NOs: 58 and 59

5' AGT TGG ACC CCT CTCTGG CTC ACT CTCTTC ACT CTT TGC ATA GGT TCT  
S W T P L W L T L P T L C I G S

GTG GTT TCT TCT GAG CTG ACT CAG GAC CCT GCT GTG TCT GTG GCC TTG GGA CAG  
V V S S E L T Q D P A V S V A L G Q

ACA GTC AGG ATC ACA TGC CAA GGA GAC AGC CTC AGA AGC TAT TAT GCA AGC TGG  
T V R I T C Q G D S L R S Y Y A S W

TACCAGCAG AAG CCA GGA CAG GCC CCT GTA CTT GTC ATCTAT GGT AAA AAC AAC V2-13  
Y Q Q K P G Q A P V L V I Y G K N N

CGG CCCTCA GGG ATC CCA GAC CGA TTCTCT GGCTCC AGCTCA GGA AAC ACA GCT  
R P S G I P D R F S G S S G N T A

TCC TTG ACC ATC ACT GGG GCT CAG GCG GAA GAT GAG GCT GACTAT TACTGT AAC  
S L T I T G A Q A E D E A D Y Y C N

TCC CGG GAC AGC AGT GGT AAC CAT CTG GTA TTC GGC GGA GGG ACC AAG CTG ACC JL2  
S R D S S G N H L V F G G G T K L T

GTC CTA GGT CAG CCC AAG GCT GCC CCT CGT GTC ACT CTG TTC CCA CCC TCC TCT  
V L G Q P K A A P S V T L F P P S S

GAG GAG CTT CAA GCC AAC AAG GCC ACA CTG GTG 3'  
E E L Q A N K A T L V CA



FIG. 22A

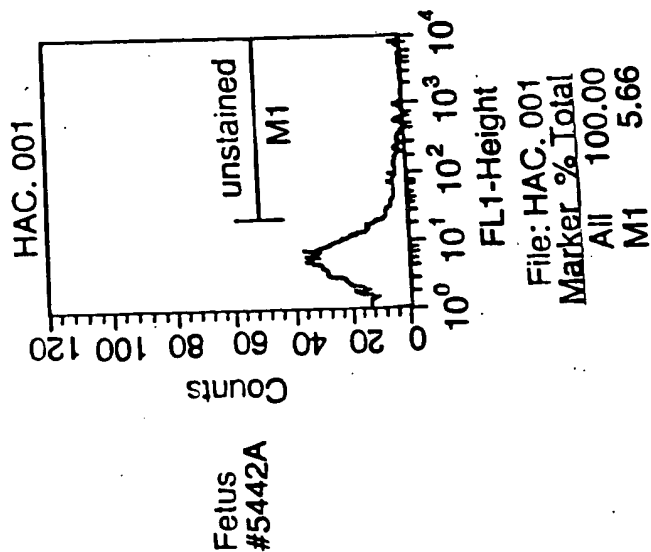


FIG. 22B

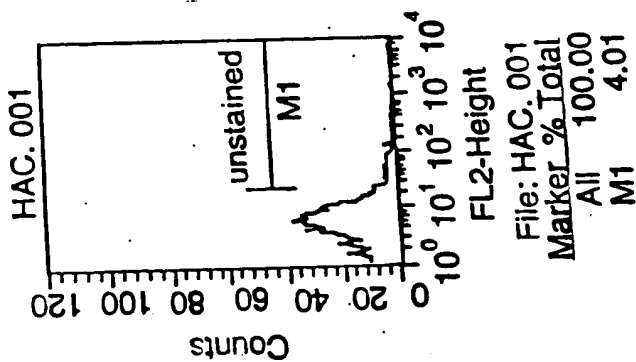


FIG. 22C

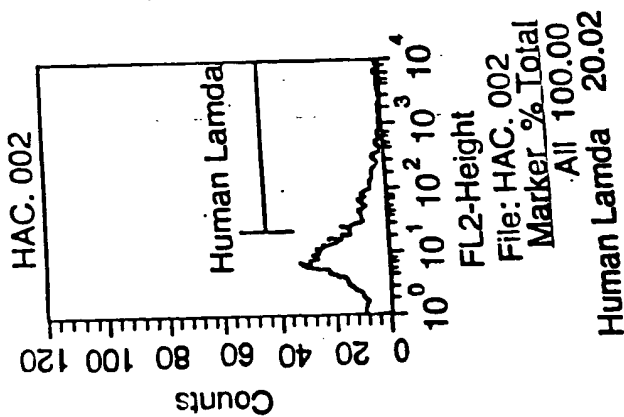


FIG. 22D

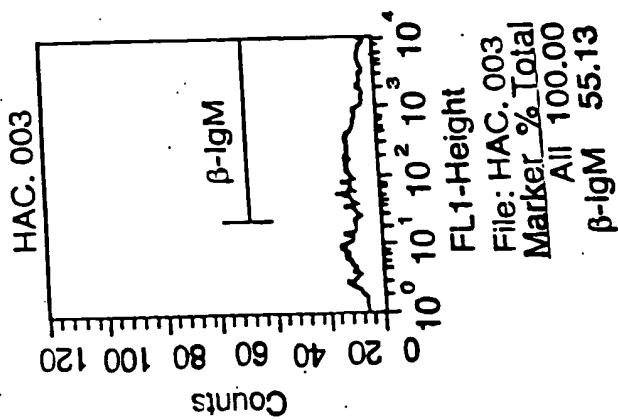


FIG. 22E

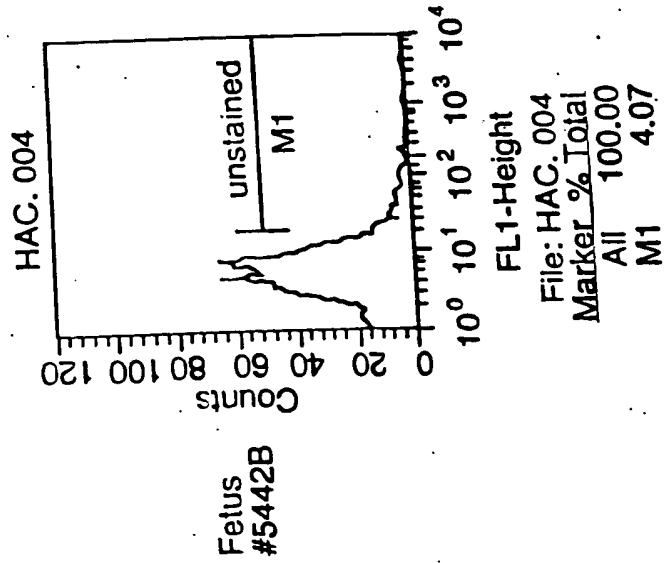


FIG. 22F

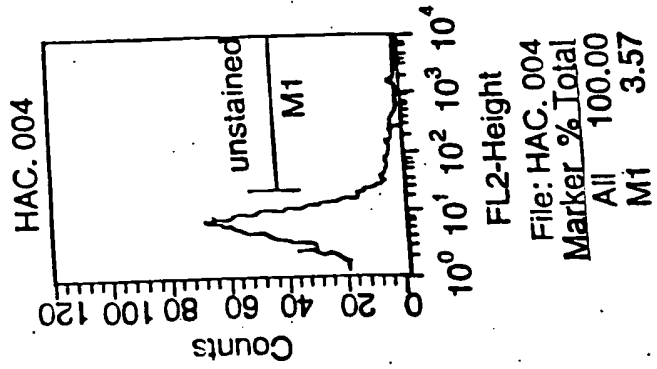


FIG. 22G

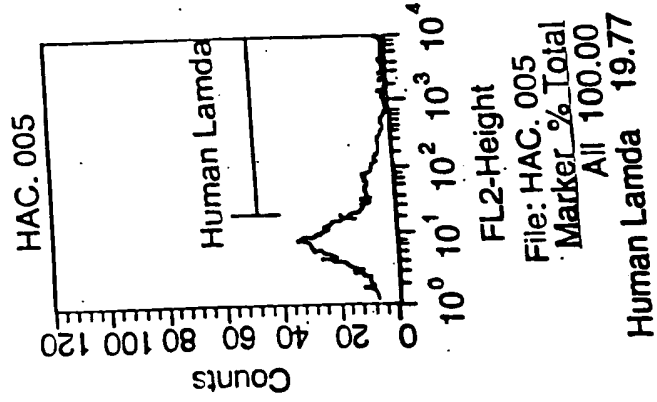


FIG. 22H

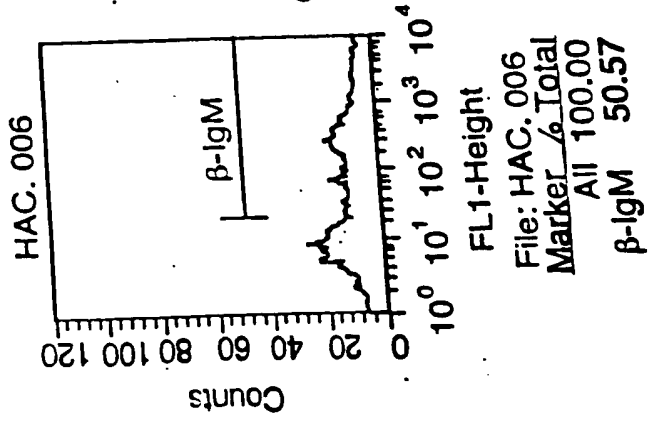


FIG. 23

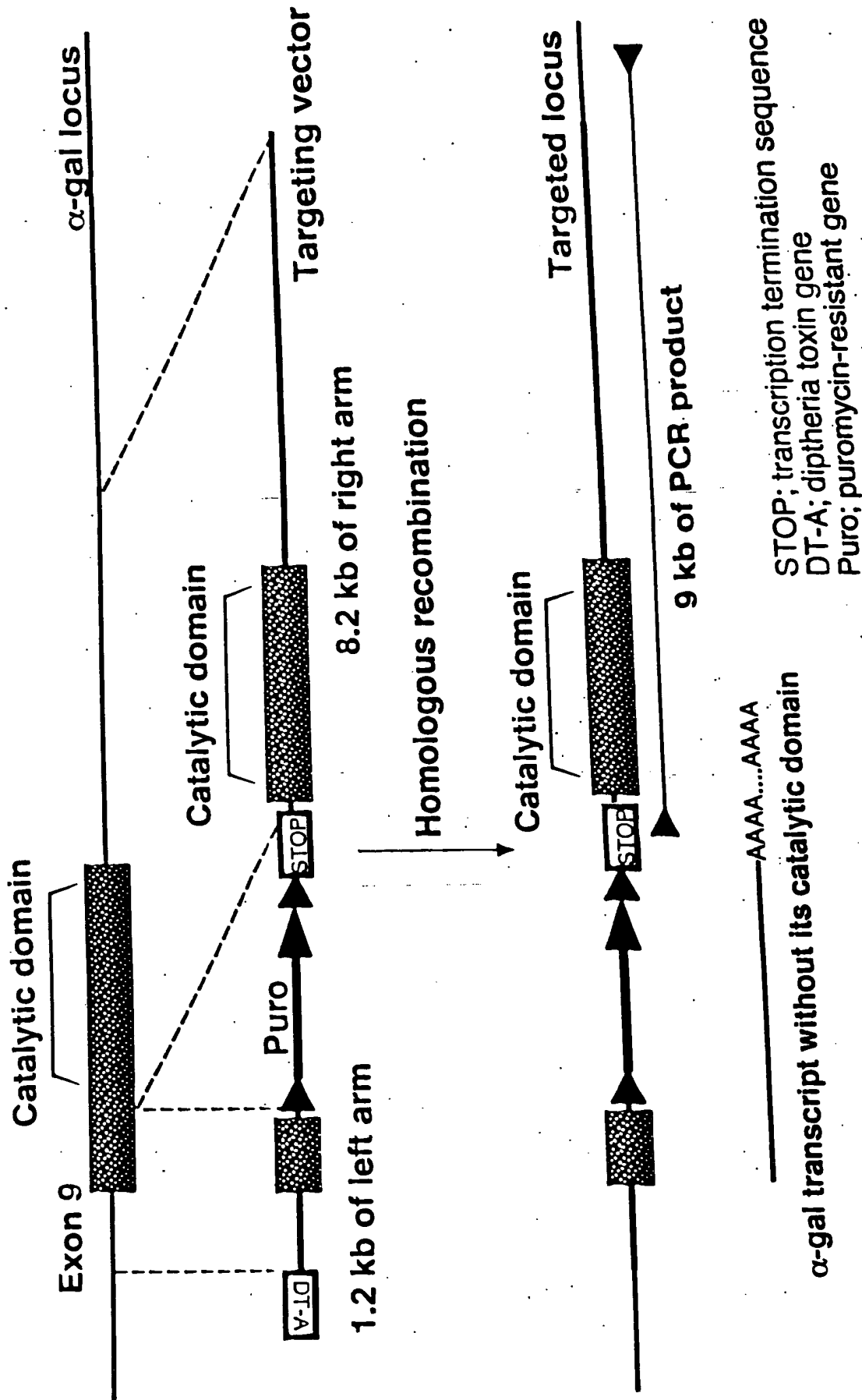


FIG. 24

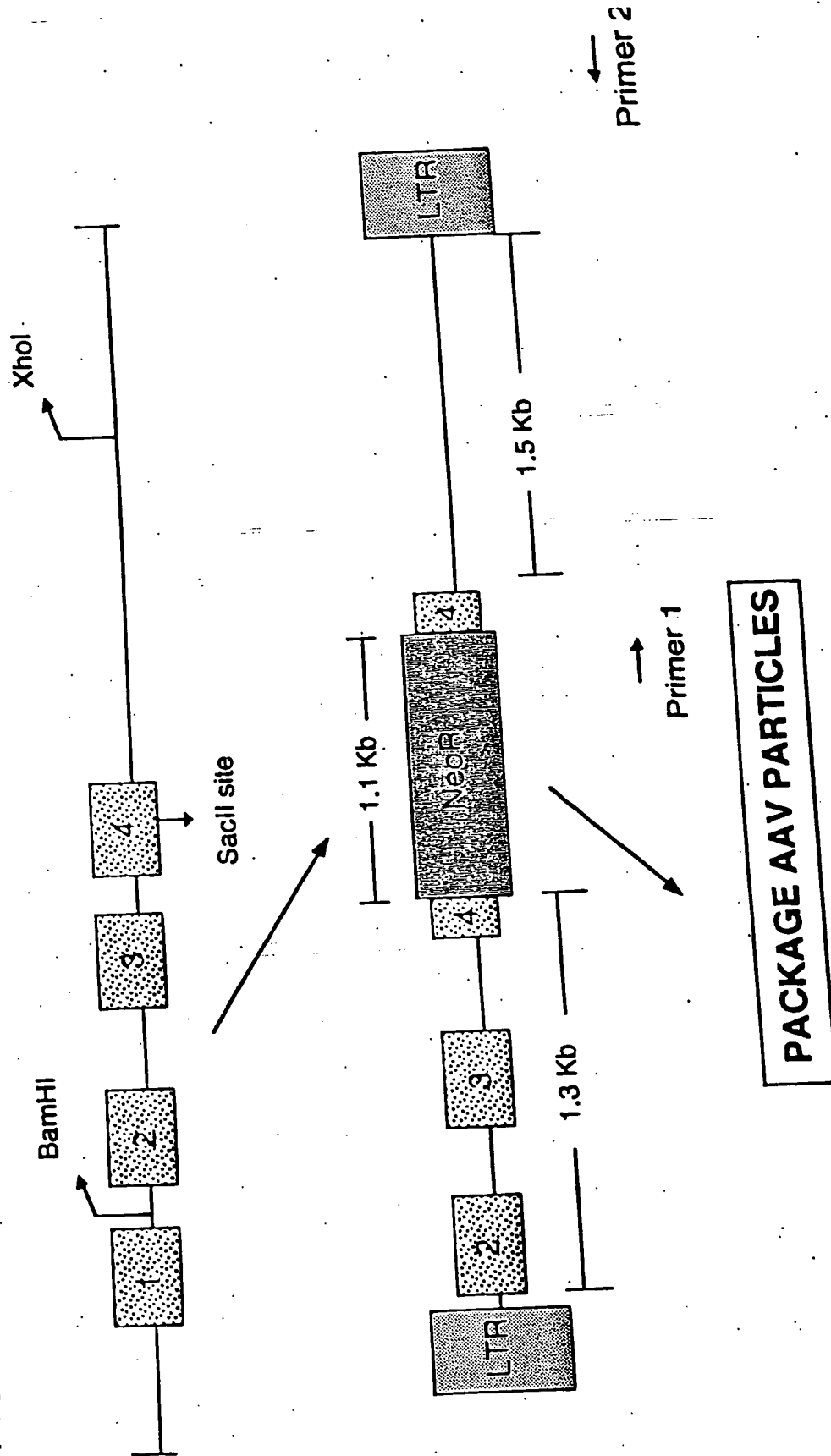


FIG. 25

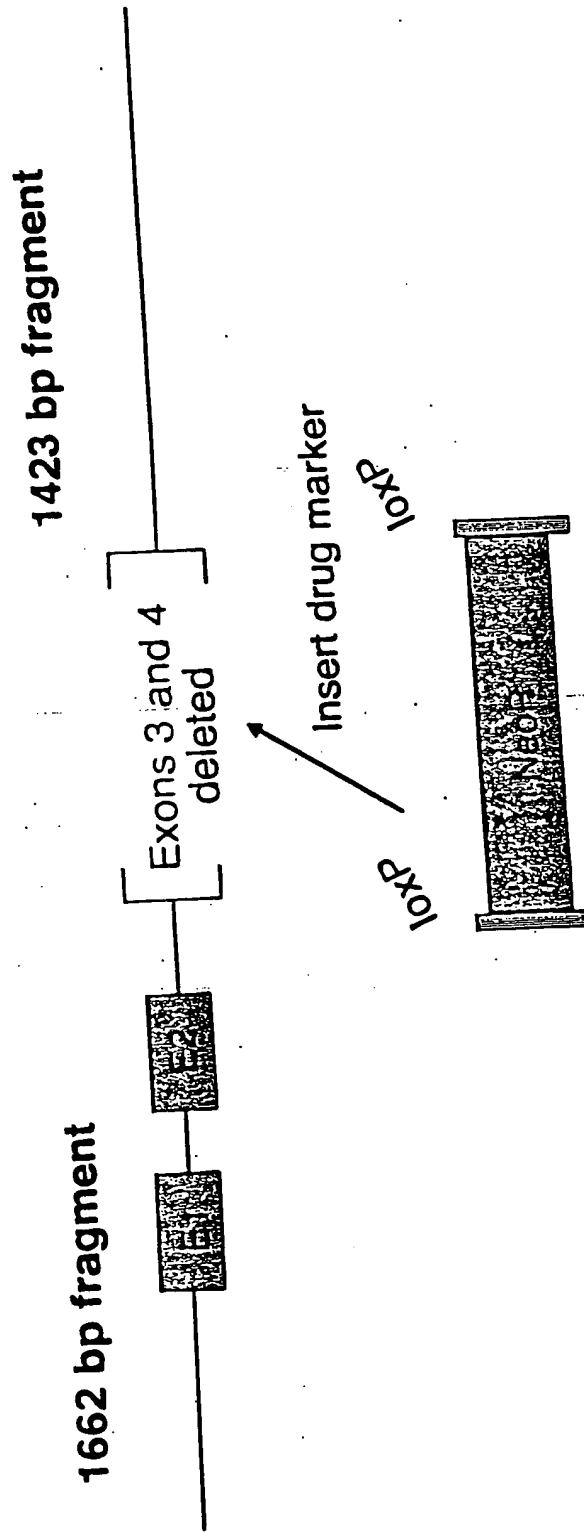


FIG. 26

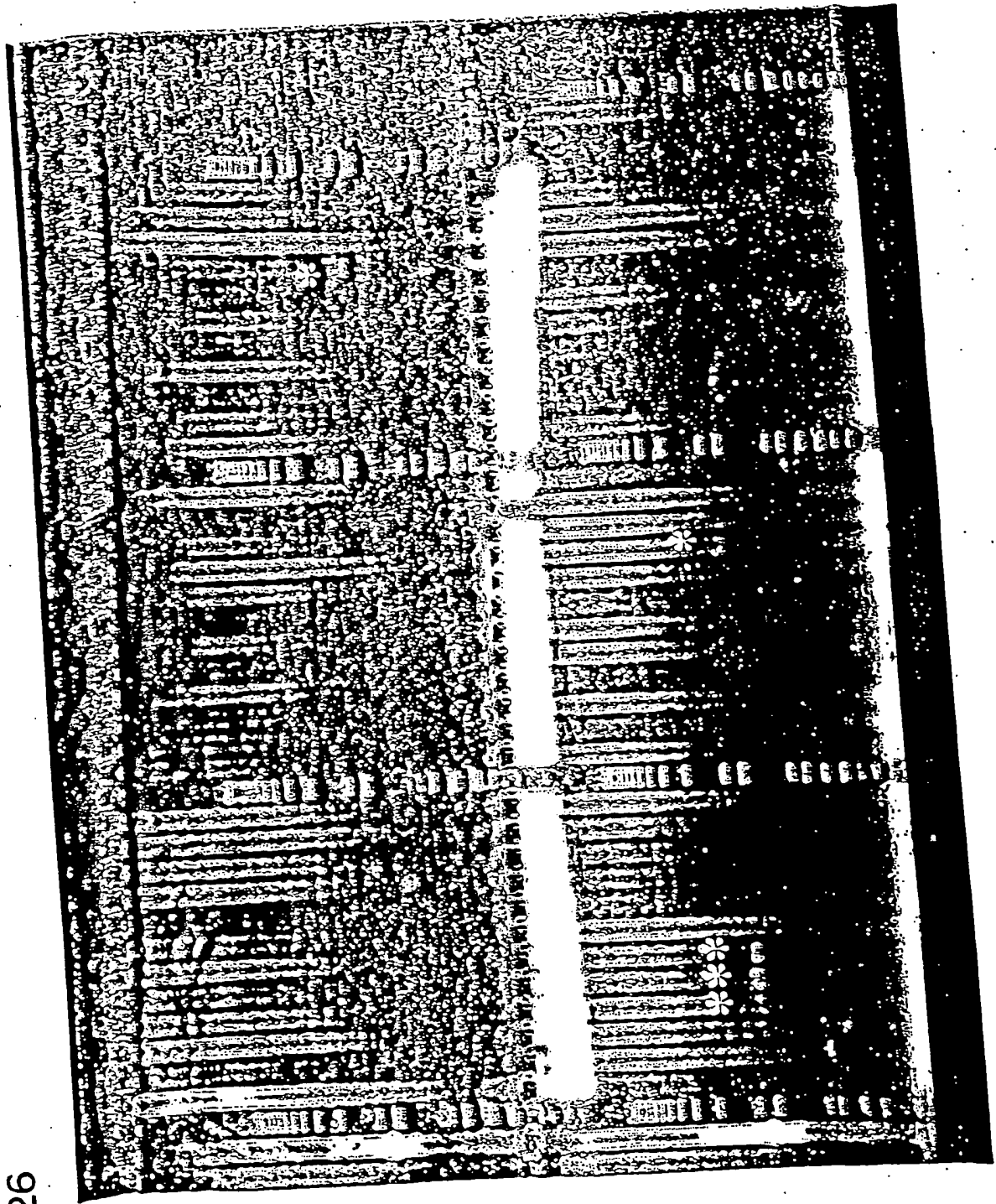


FIG. 27

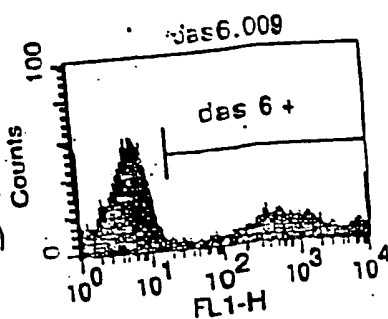
NT, ET and pregnancies : Delta HAC regenerated fibroblasts											
Cell line ID	Total NTs In culture	No of Blast (%)	No of Blast Transferred	No Recios	Pregnancy status						
					40 d	60 d	90 d	120 d	150 d	180 d	210 d
D5968	174	34 (28)	27	17	3	3	3	3	3	3	3
D6045	218	10 (7)	8	4	1	1	1	1	1	1	1
D6045	122	20 (23)	12	9	1	0	0	0	0	0	0
D6032	161	12 (18)	14	7	3	3	3	2	2	2	2
D6032	188	15 (11)	11	11	3	0	0	0	0	0	0
D6032	198	20 (14)	16	10	1	1	1	1	1	1	1
D6032	200	17 (12)	12	8	2	2	2	2	2	2	2
D6032	180	11 (8)	10	5	3	1	1	1	1	1	1
D6032	135	22 (23)	22	11	2	2	1	1	1	1	1
D5968	140	35 (36)	25	13	2	2	1	1	1	1	1
D5968	180	30 (24)	26	13	2	2	1	1	1	1	1
D6045	170	46 (39)	32	16	4	4	4	4	4	4	4
D6045	80	7 (13)	1	1	0	0	0	0	0	0	0
D6045	80	9 (12)	3	2	1	1	1	1	1	1	1
D6045 SLOT	108	8 (15)	2	1	0	0	0	0	0	0	0
D6045	78	12 (13)	7	3	2	2	2	2	2	2	2
D6045 SLOT	128	6 (18)	3	2	2	2	2	2	2	2	2
D6045	47	3 (4)	3	2	2	2	2	2	2	2	2
D6045 SLOT	112	22 (33)	18	9	1	1	1	1	1	1	1
D6045	120	11 (16)	2	1	1	1	1	1	1	1	1
D6045 SLOT	100	15 (27)	18	8	1	1	1	1	1	1	1
D6045	78	0	2	1	1	1	1	1	1	1	1
D6045 SLOT	91	16 (23)	10	5	1	1	1	1	1	1	1
D6045	98	16 (22)	10	5	1	1	1	1	1	1	1
D6045 SLOT	104	24 (27)	8	4	1	1	1	1	1	1	1
D5968	128	10 (22)	8	4	1	1	1	1	1	1	1
D5968 SLOT	65	22 (33)	14	7	1	1	1	1	1	1	1
D5968	120	13 (19)	8	3	1	1	1	1	1	1	1
D5968 SLOT	95	17 (25)	20	10	1	1	1	1	1	1	1
D5968	98	14 (22)	12	6	1	1	1	1	1	1	1
D5968 SLOT	63	1 (11)	1	3	1	1	1	1	1	1	1
D	13	8 (18)	4	3	1	1	1	1	1	1	1
SLOT	63	4 (5)	1	3	1	1	1	1	1	1	1
D	108	1 (1)	1	3	1	1	1	1	1	1	1
SLOT	100	10 (18)	10	6	1	1	1	1	1	1	1
D	90	13 (17)	13	6	1	1	1	1	1	1	1
SLOT	110	10 (18)	10	1	1	1	1	1	1	1	1
D	90	5 (9)	5	1	1	1	1	1	1	1	1
SLOT	83	20 (27)	20	9	1	1	1	1	1	1	1
D	105	7 (13)	7	2	1	1	1	1	1	1	1
SLOT	78	7 (11)	7	4	1	1	1	1	1	1	1
D	88	9 (14)	9	4	1	1	1	1	1	1	1
SLOT	93	20 (33)	20	10	1	1	1	1	1	1	1
D	85	4 (7)	4	2	1	1	1	1	1	1	1
SLOT	77	215 (19)	481	258							

Summary	No of Pregnancies
Preg Status	9
> 40 d	2
> 60 d	4
> 120 d	3
> 180 d	3
> 210 d	3
Total	21

A

876

(Control)

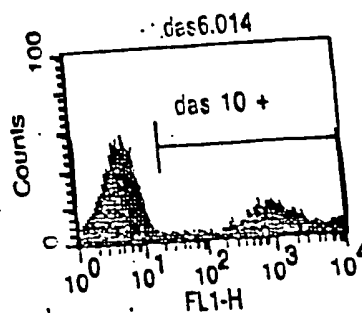


% Total

100.00

26.61 %

F



% Total

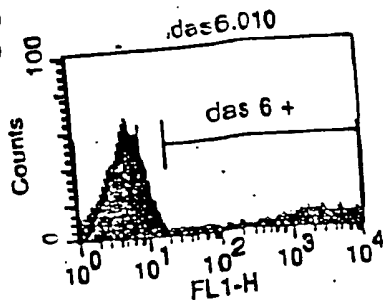
100.00

29.47 %

B

4904

(Control)

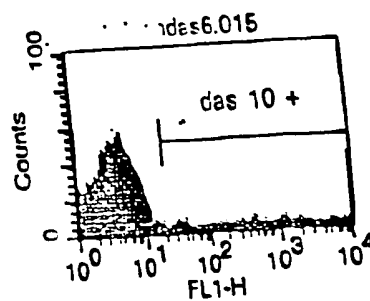


% Total

100.00

19.62 %

G



% Total

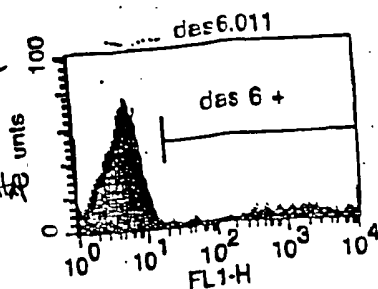
100.00

12.43 %

C

5961

Experimental

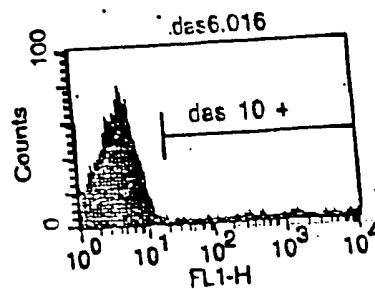


% Total

100.00

7.78 %

H



% Total

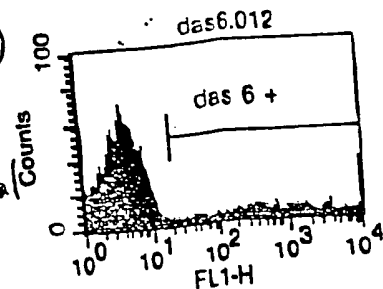
100.00

2.54 %

D

5971

Experimental

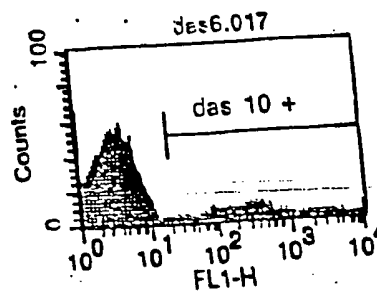


% Total

100.00

11.80 %

I



% Total

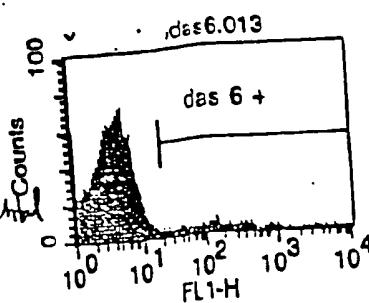
100.00

13.77 %

E

5990

Experimental

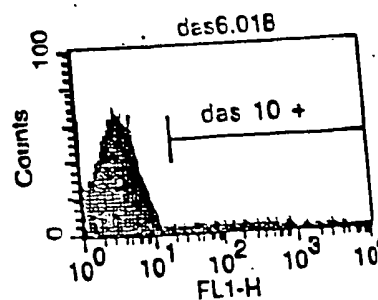


% Total

100.00

3.95 %

J



% Total

100.00

3.99 %

Figures 28A-28J



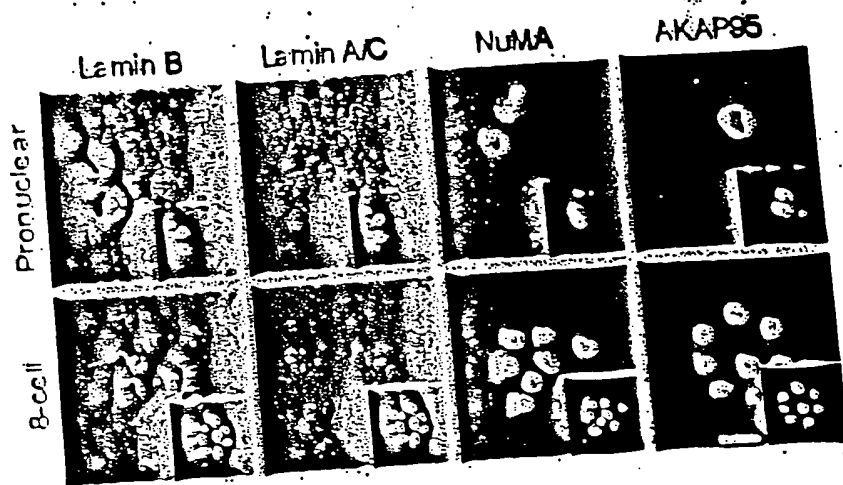


FIGURE 29A

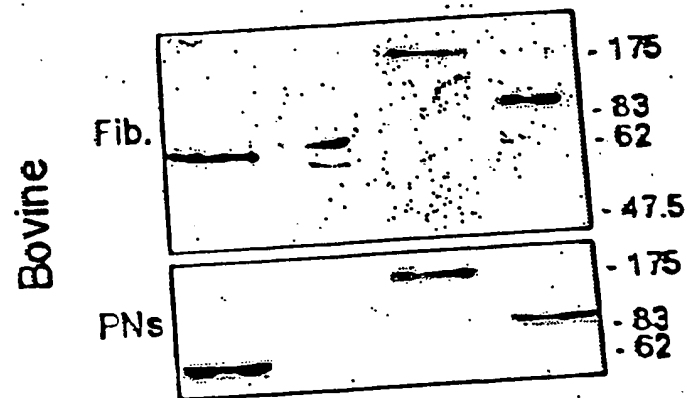


FIGURE 29B

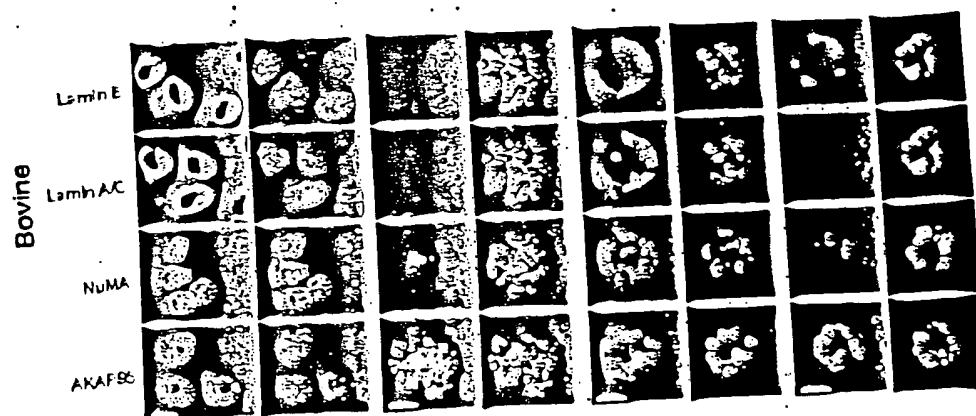


FIGURE 30

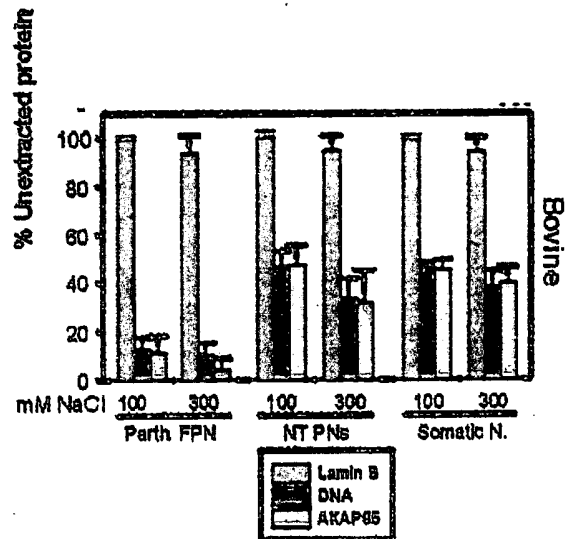


Figure 31

FIGURE 32

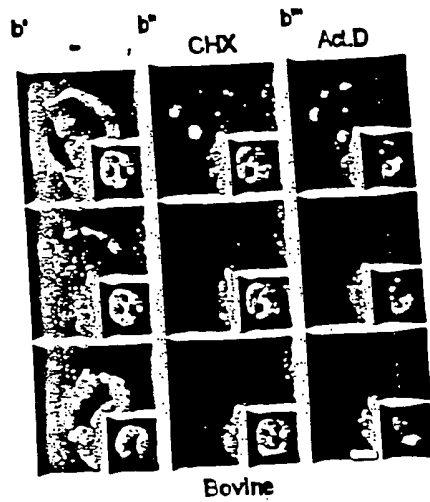
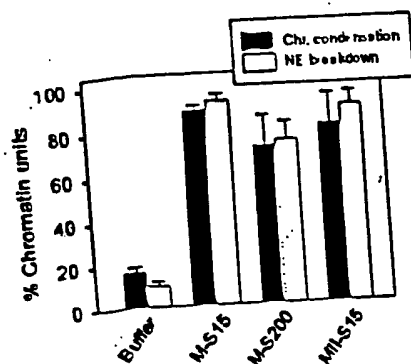
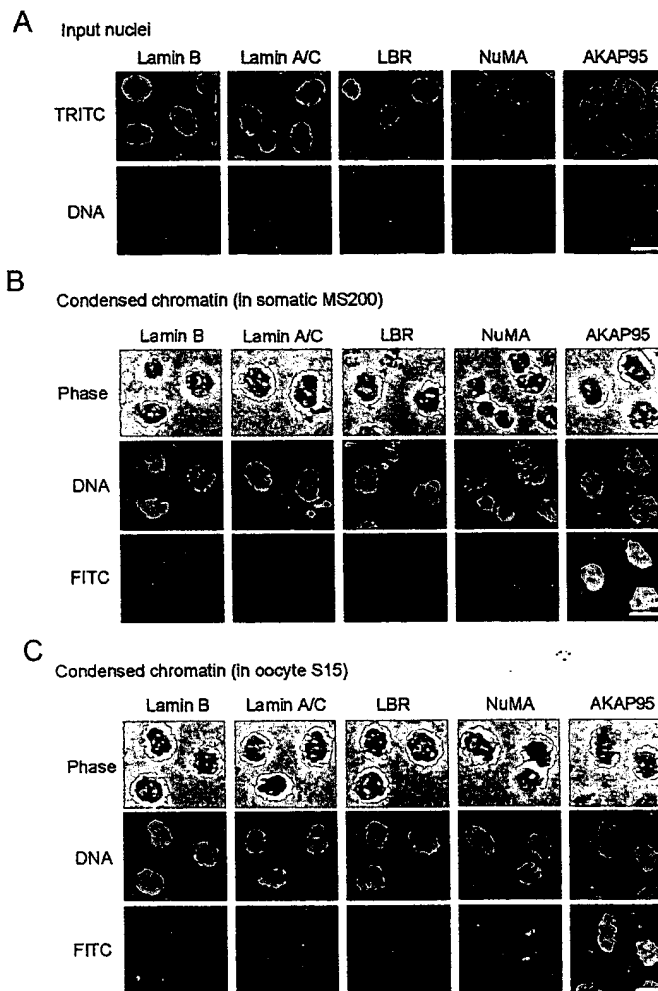


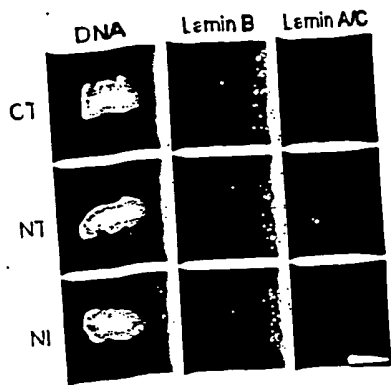
FIGURE 33



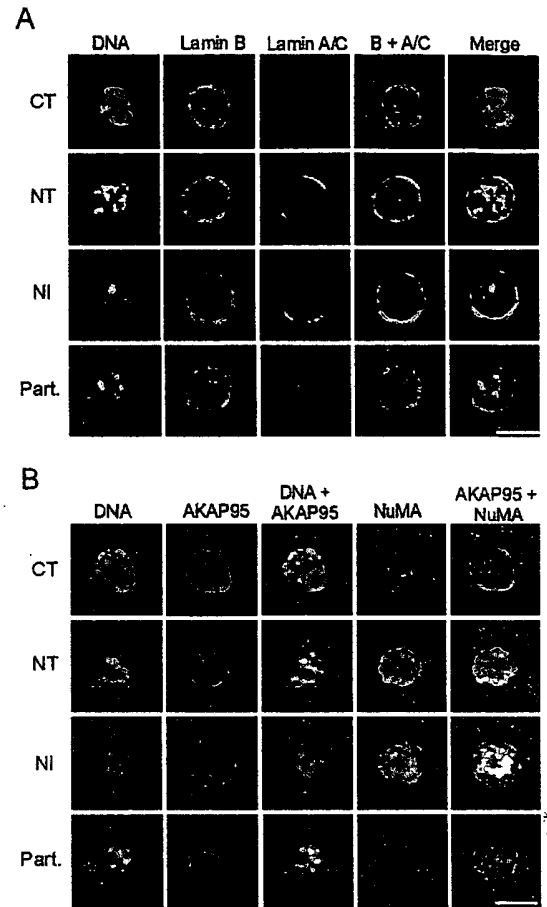


Figures 34A – 34C

FIGURE 35







Figures 36A and 36B

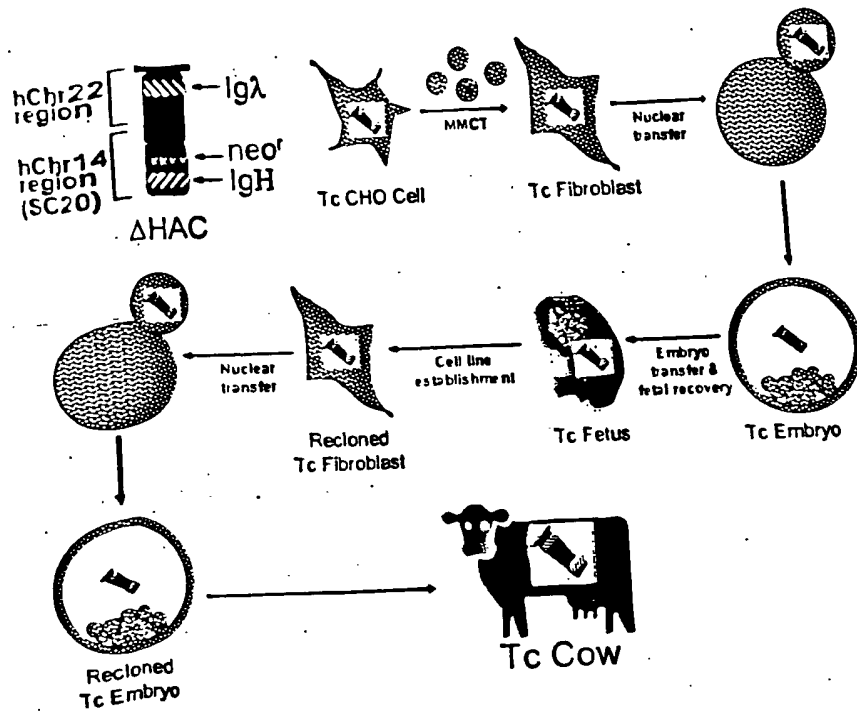


FIGURE 37



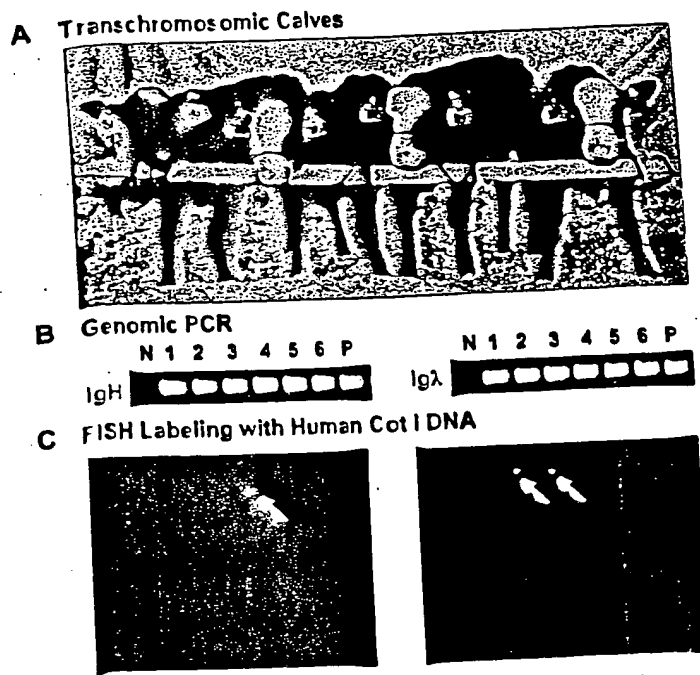
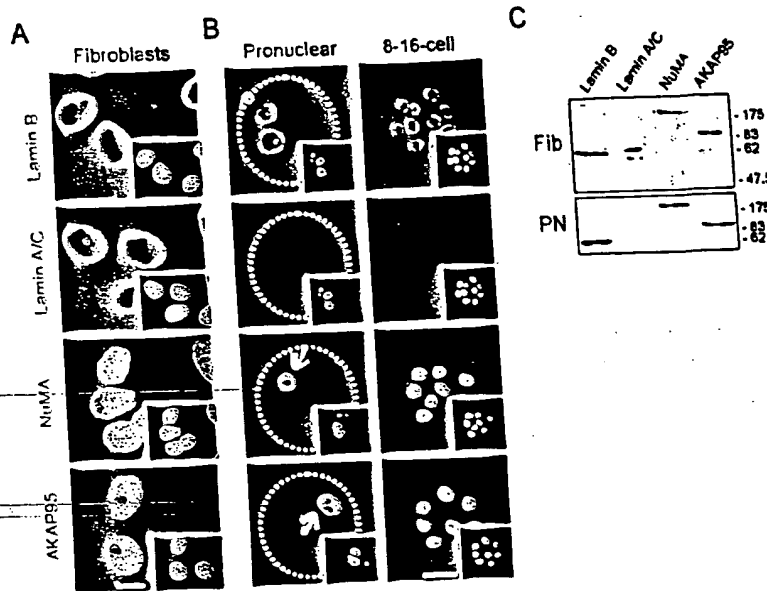
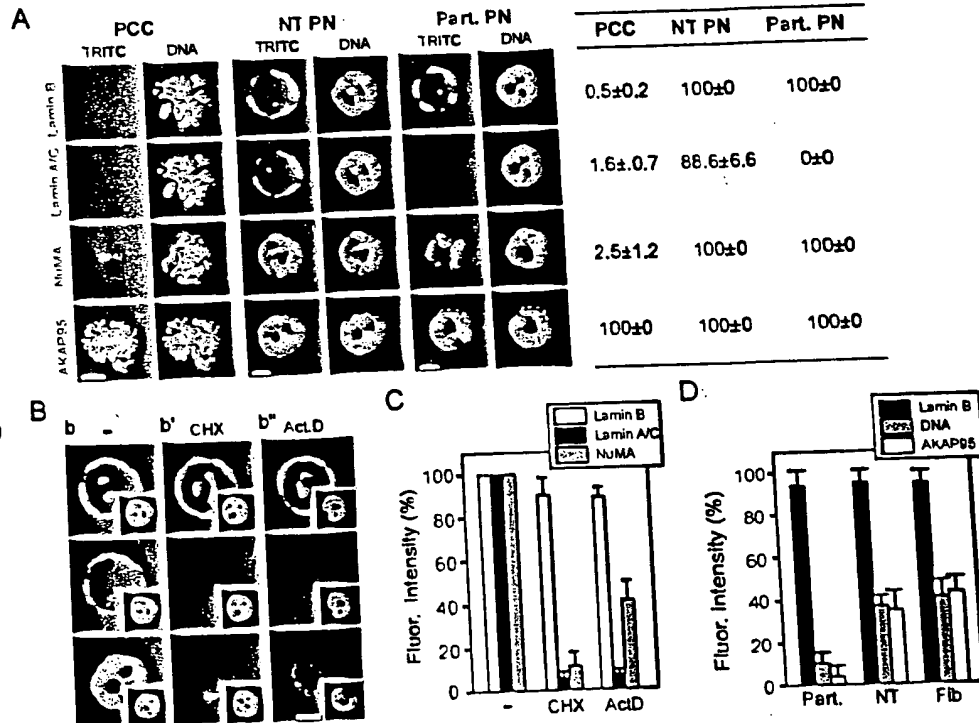


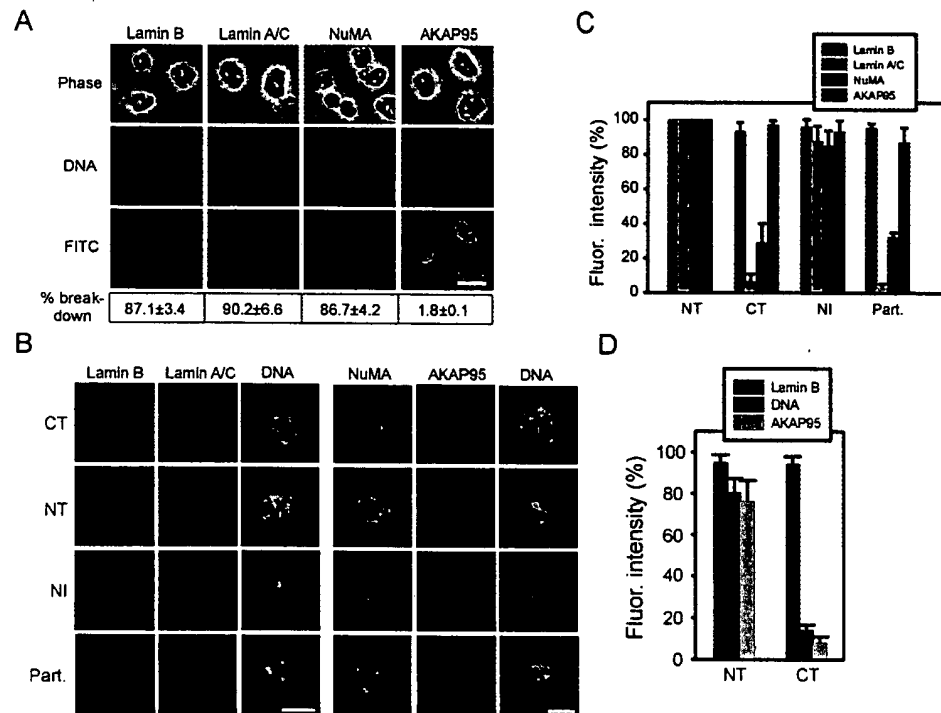
FIGURE 39 A-C

Figs. 40A-40C



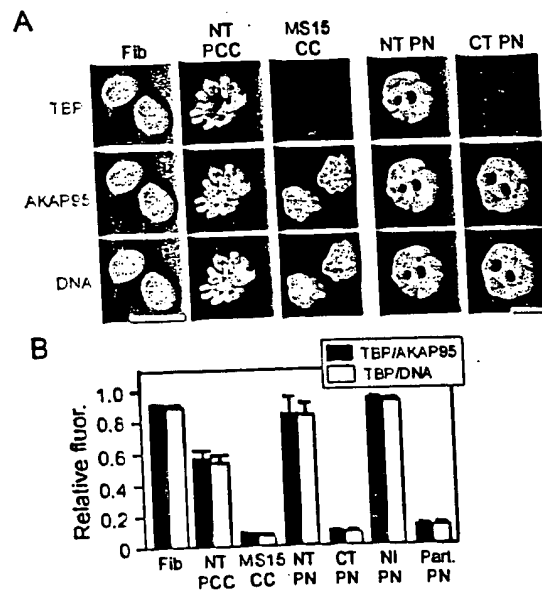
Figs. 41A-41D





Figs. 42A-42D

Figs. 43A and 43B



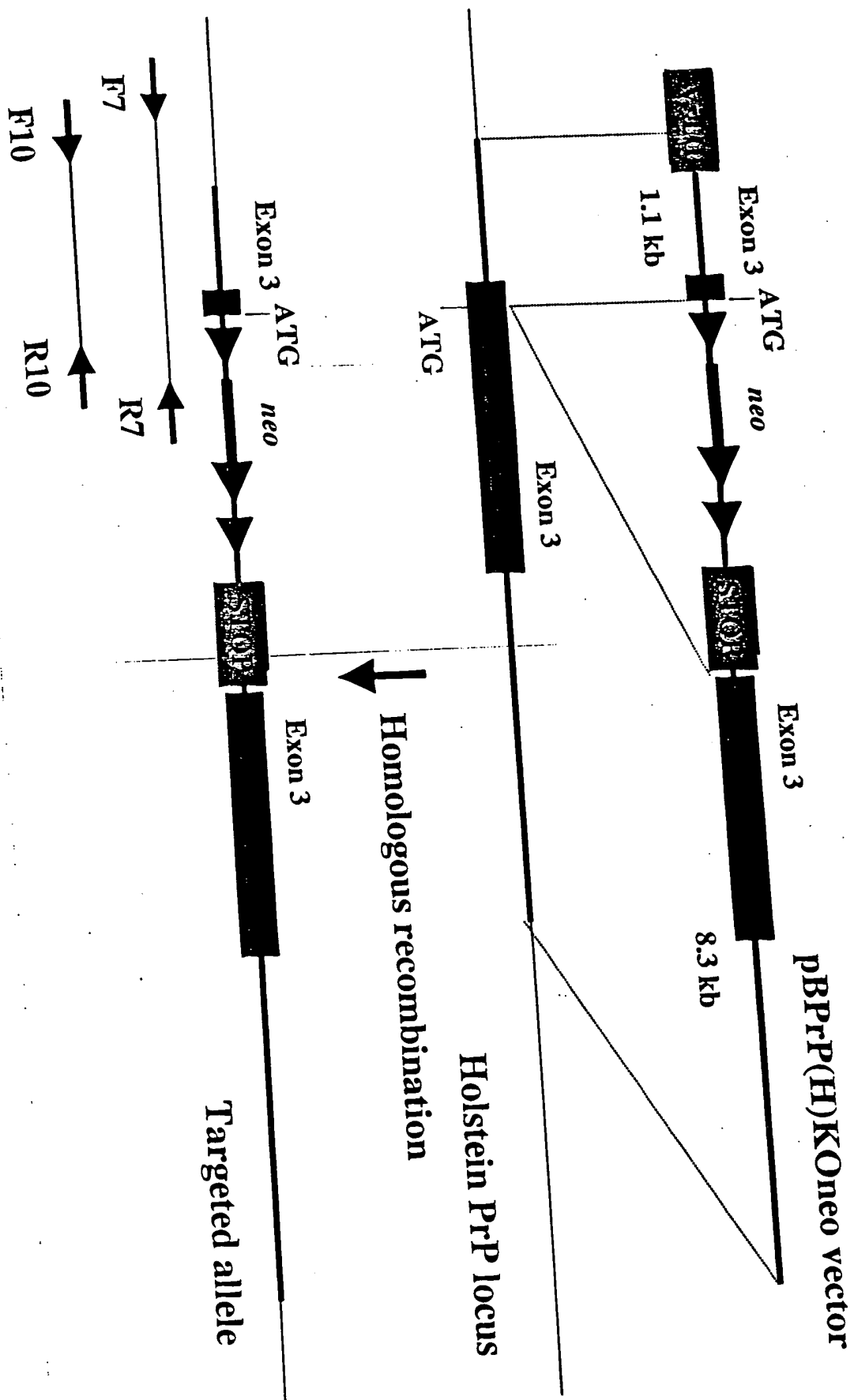


Fig. 44A



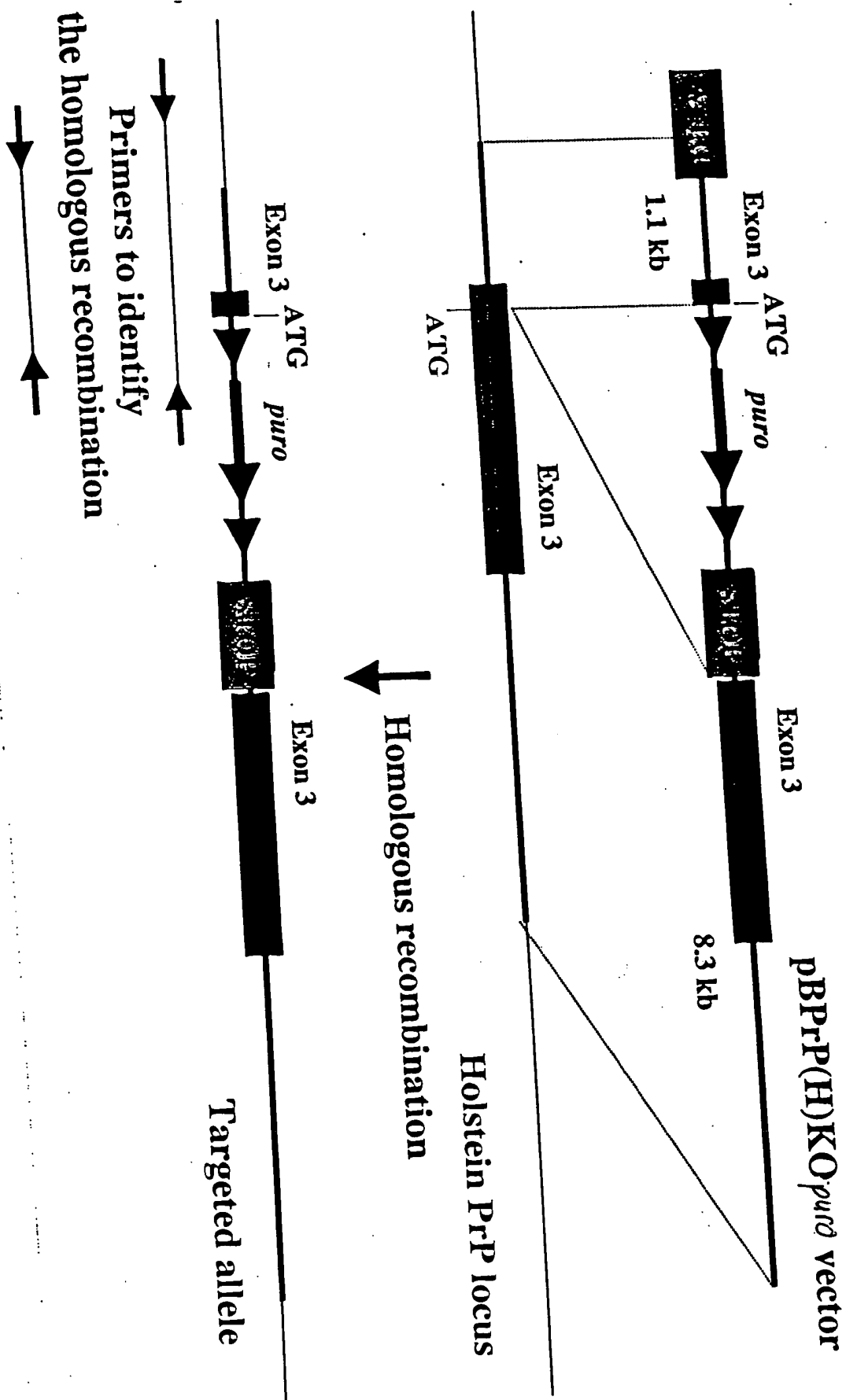
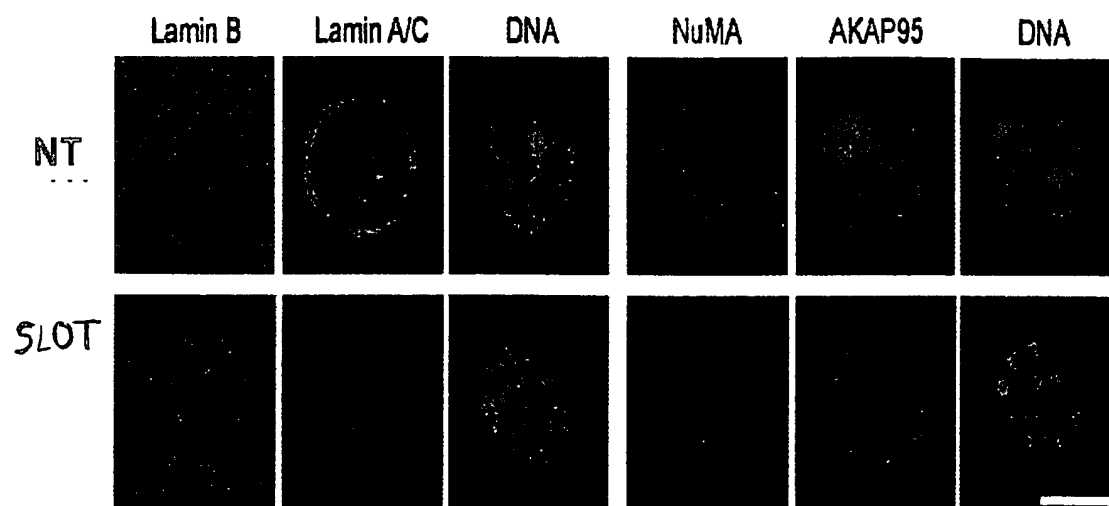


Fig. 44B

Cell line	No of screened clone	Primers F7 x R7	Primers F10 x R10	Frequency
Holstein	94	51	51	>50 %
Holstein x Jersey	141	75	75	>50 %

Fig. 44C

# Figure 45A



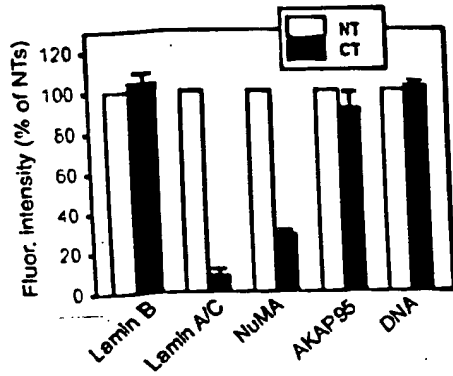
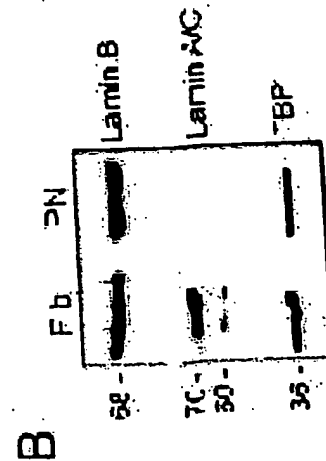
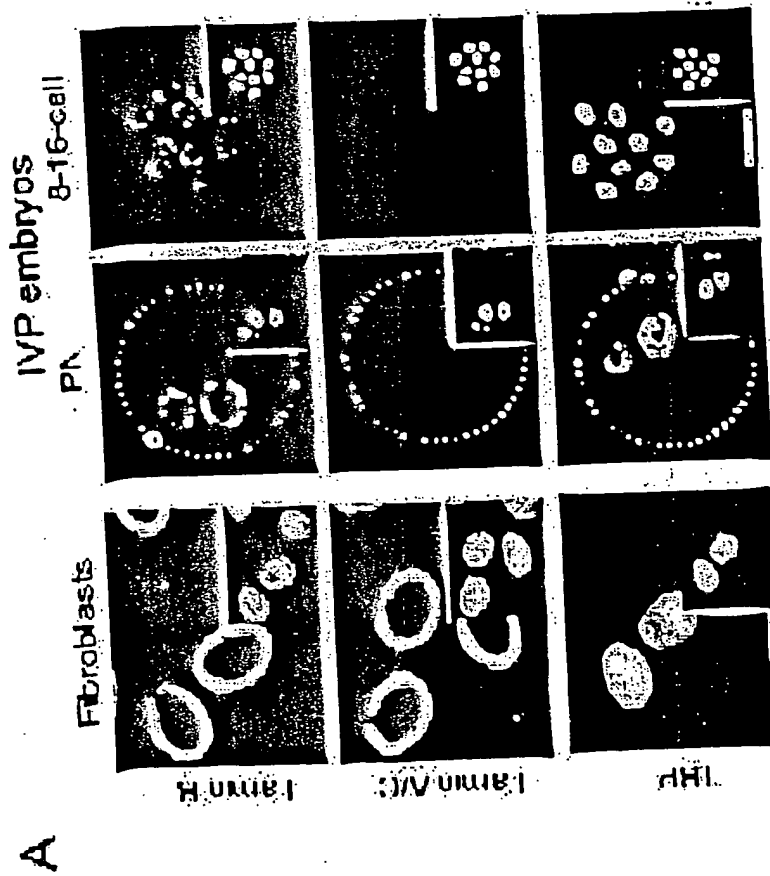
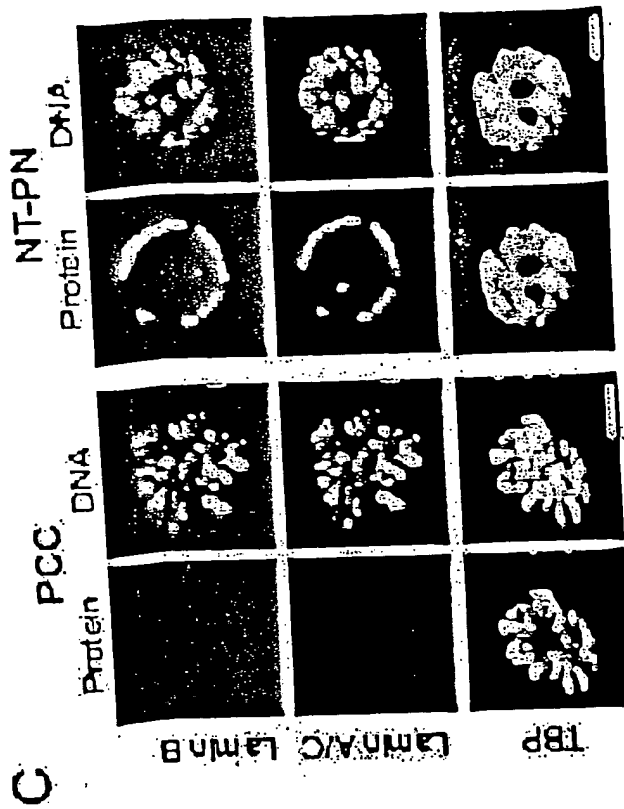


Figure 45B



Figures 46A-46C

46D

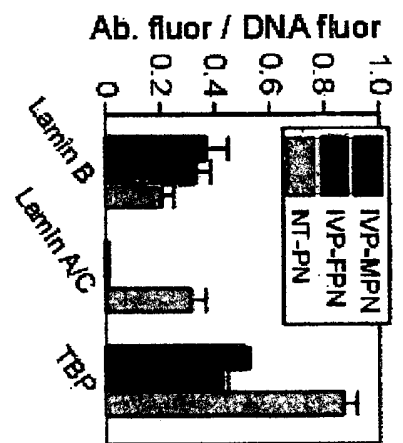


Figure 46D

47A

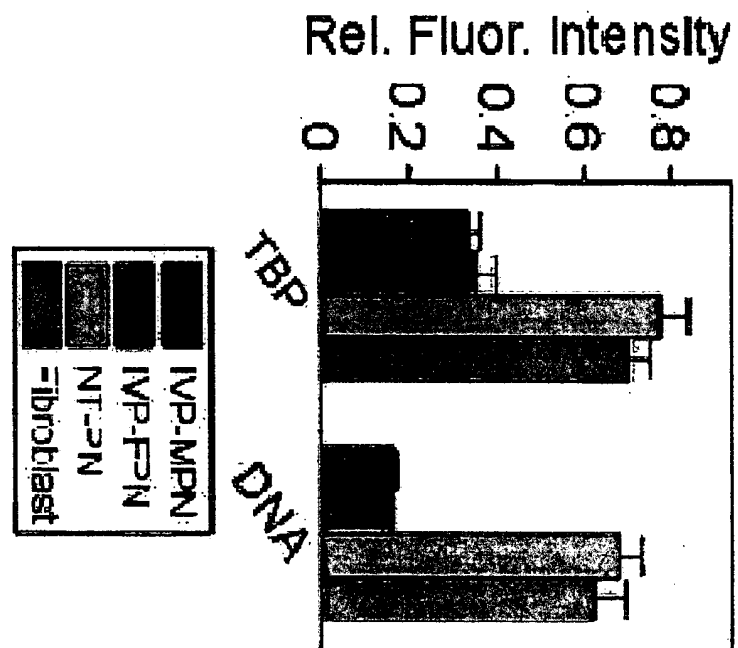


Figure 47A

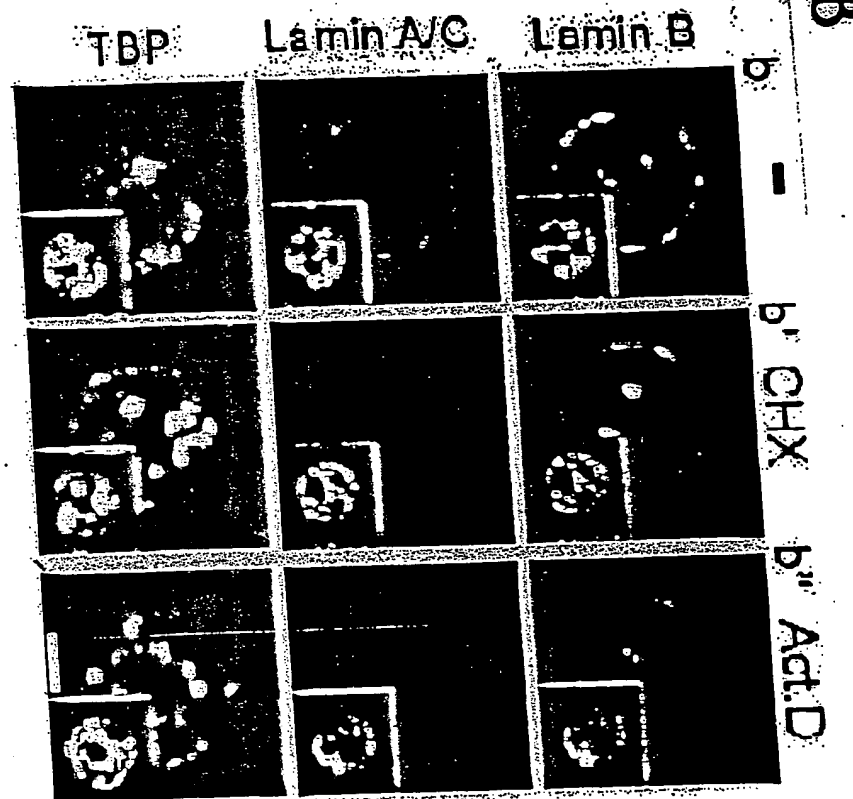


Figure 47B



47C

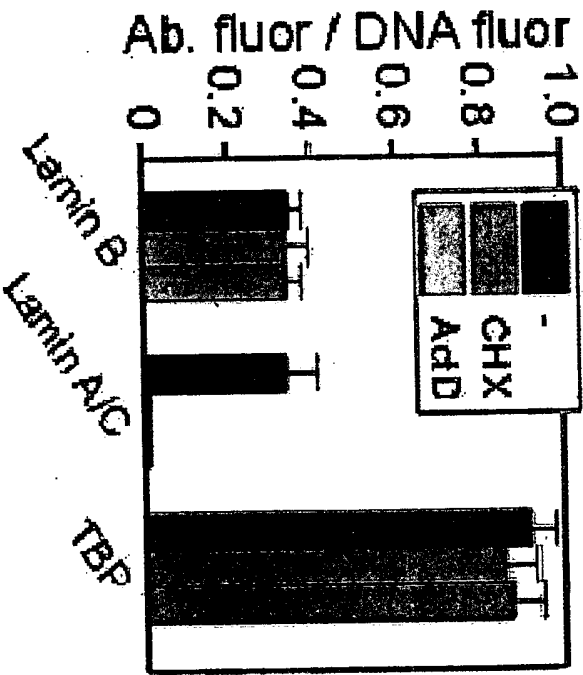


Figure 47C

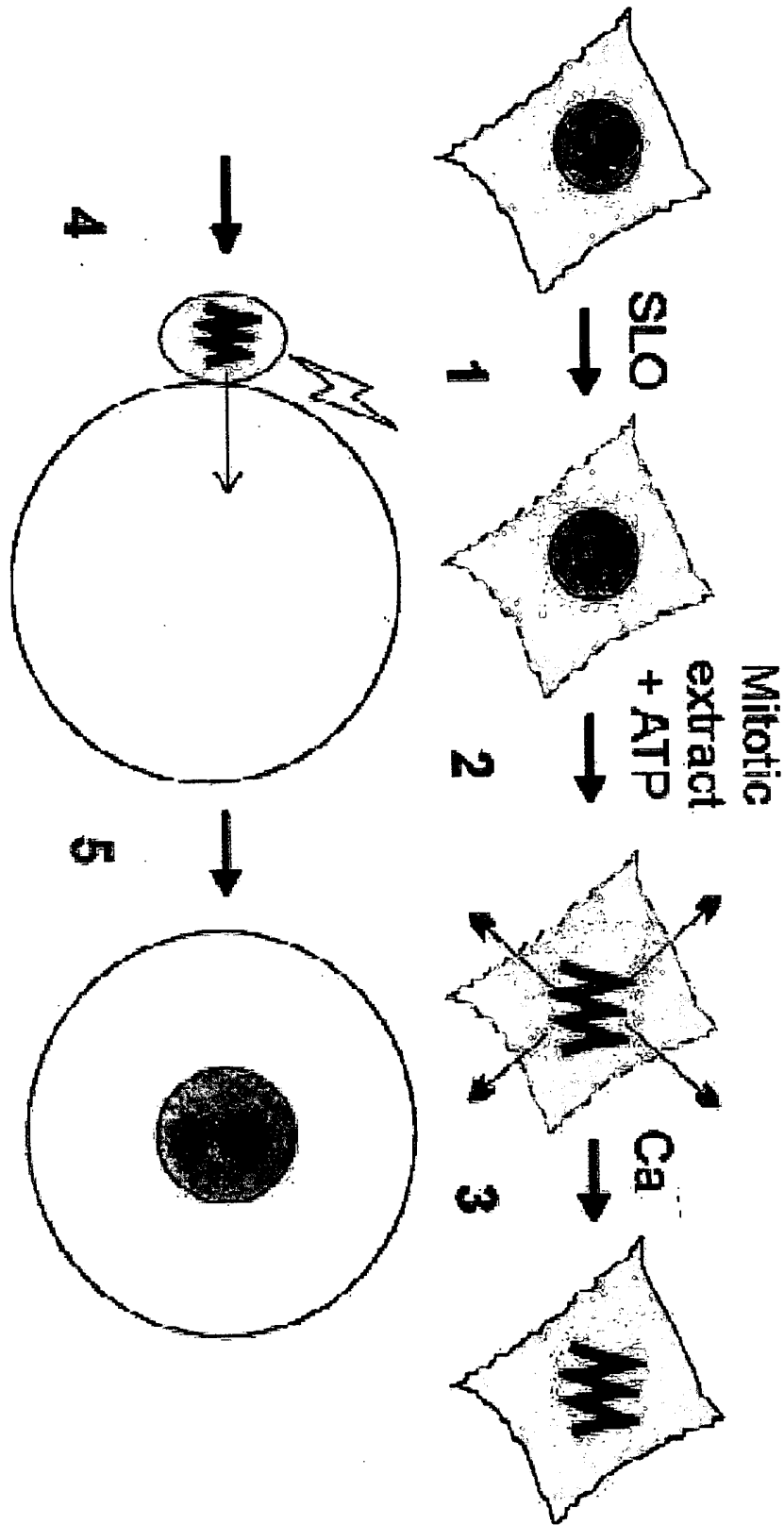


Figure 48

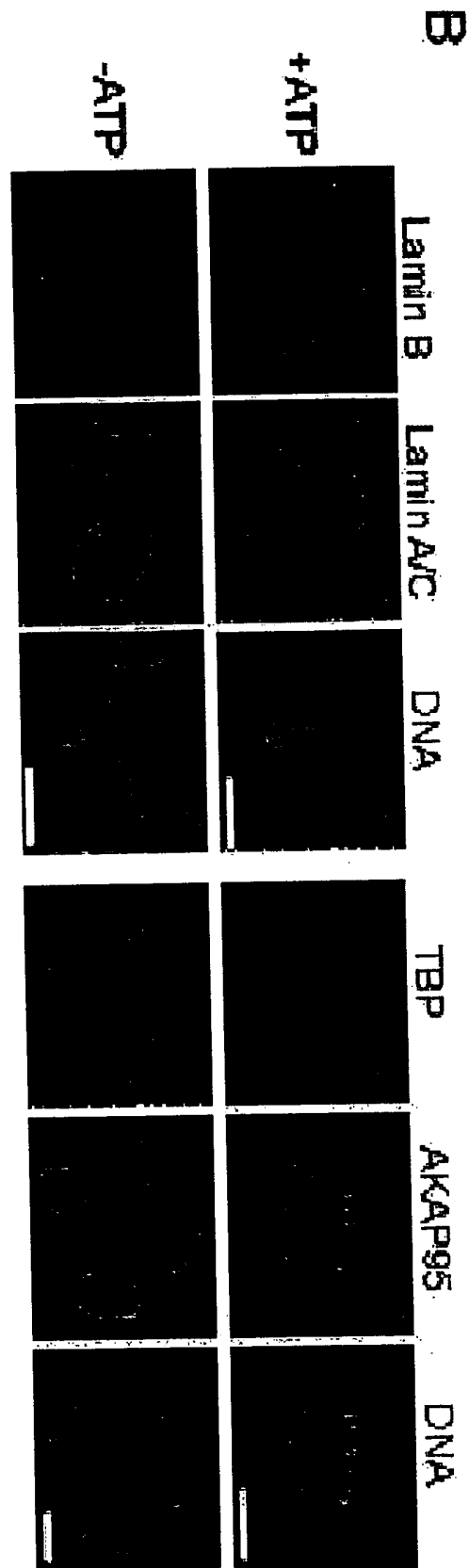


Figure 49

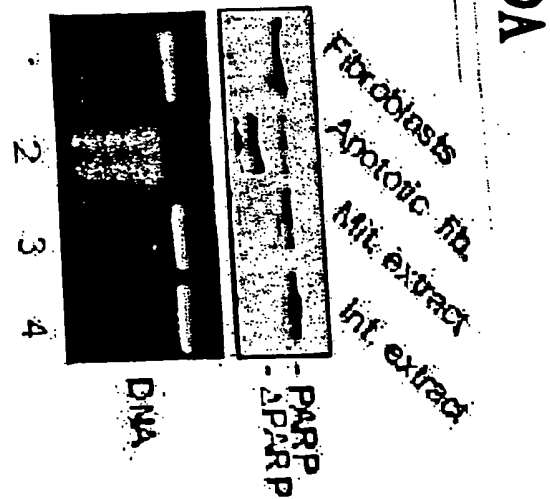


Figure 49A

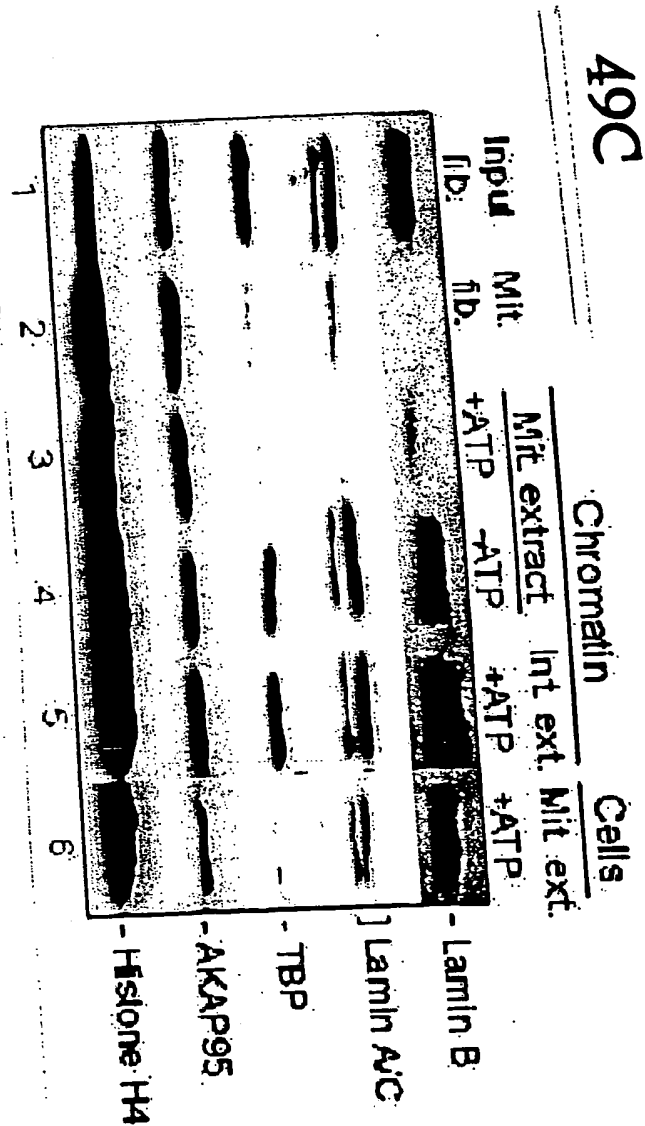
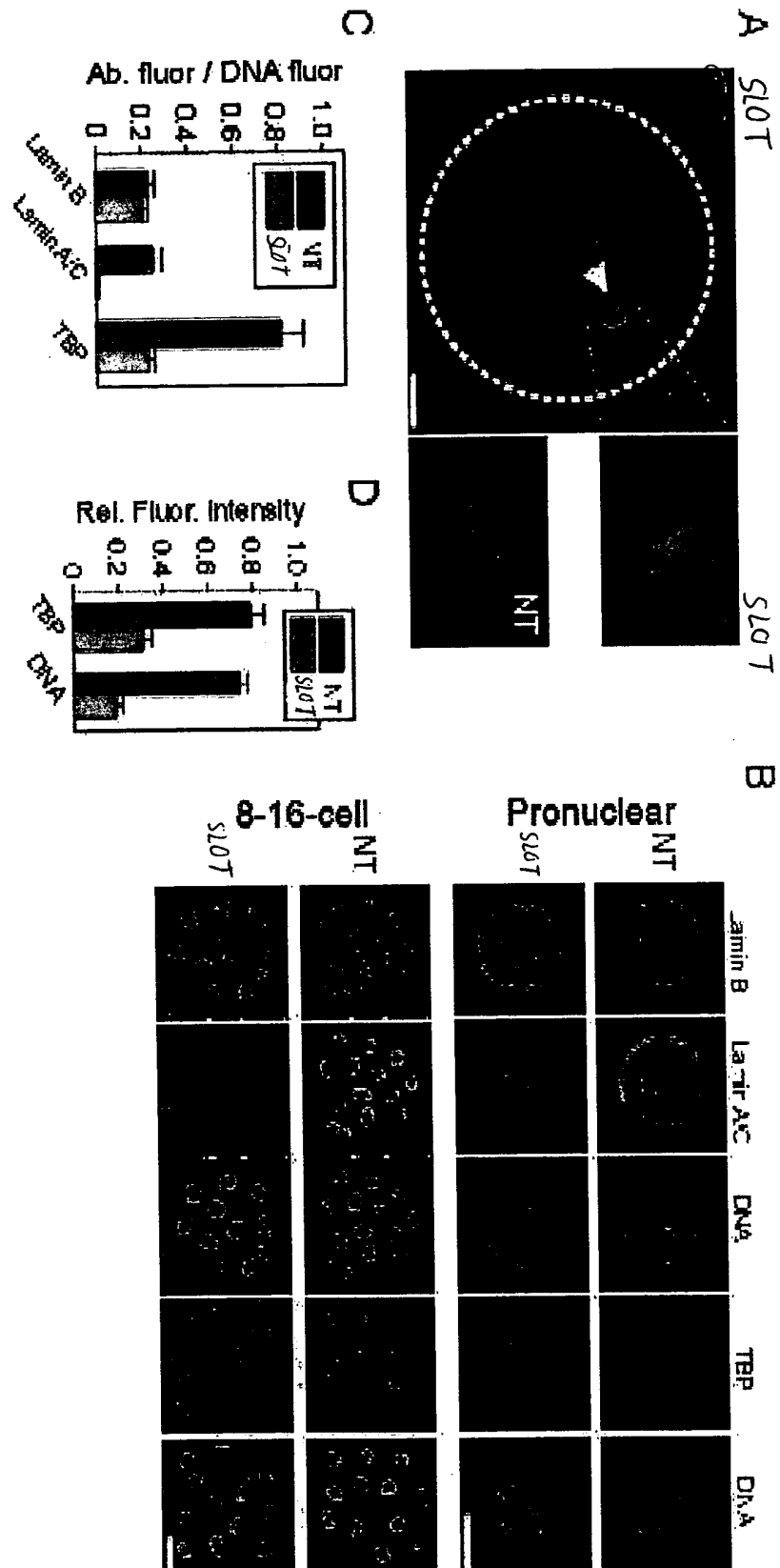


Figure 49C



Figures 50A-50D

51A

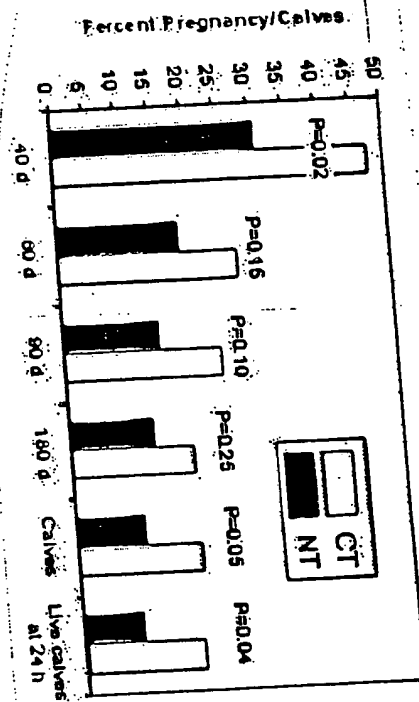


Figure 51A

Title: TRANSGENIC UNGULATES HAVING REDUCED  
PRION PROTEIN ACTIVITY AND USES THEREOF

Applicant(s): James M. Robl et al.

Filing Date: November 10, 2003

Serial No.: N/A

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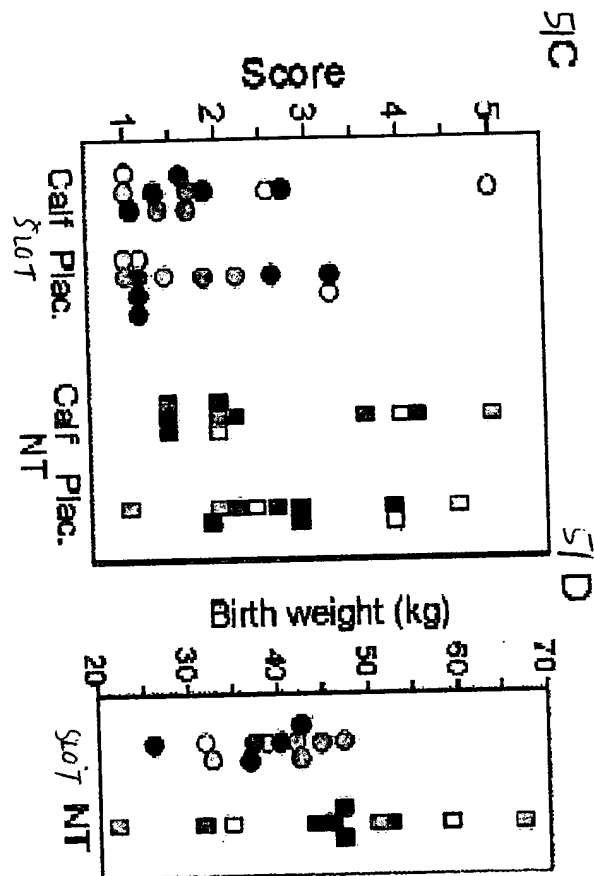
Customer No.: 21559

51B



Figure 51B





Figures 51C-51D

Figure 51E

